

TCACGTAATA AGCGTATCTA GAAATTATGAT GATTACTCTG CCCAAACTTC CTCCTGGCGGT TGCCGTCCGA GCGGCGGTAA TGTCTCTCA GCCCATGCCC
ACTGCATTTT TCCCATAGAT CTTAATACTA CTAAATGAGC GCGTTTGAG GAGACCGCCA ACGGCAGCGT CGCCCGCATT ACAGACAGAT CCGGTACCGG
MetMe tIleThrIeu ArgLySLeuP roLeuAlaVa lAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla
^Start of lamb signal sequence

GGTCCCGAAA CTCCTGTGCGG TGCCTGAACCTG GTTGAACCTC TGCAGTTCCT ATGTGCTGAT CGAGGCTTC TGTTCACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTTGAC CAACTGGCAG ACGTCACAGA TACACCACTA GCTCCGAAG ACAAAGTTT TGGCTGACCC CGACTAGGA
GlyProGlnT hTLeucySGI yAlaGluLeu ValAspAla euclnPhenA IcySclasp ArgGlyPhel euphenAonly atrothrely AlaclySerSer
*Start of IGF-I (Y24L,Y31A)

CCCTCTCGTC TGTCTCCCAAG ACTGGTAATTC TTGACGGAATG CTGCTTTTCGT TCTTGGCAAC TGGCGTCGCTT GGAAATGTAT TGGCTCTCCCC TGAAACCCGC
GGAGACGACG ACGAGGGGTC TGACCATTAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACCGACGACA CCTTTACATA ACGCAGAGGG ACTTTGGGCG
SerArgar galProlin ThrIyIiev alaSpIucy scySthearg SerCySaSpI euArgArgIe uGluMetCyr CysAlaProl euIysProlaIa

TAATATCTGCT TAGAAGCTCC TAAAGCTCGG TTGCGGCGGG GCGTYYTYYTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATTAAGCTTT AATGGGGTAG
ATTTAGACCA ATCTTCGAGG ATTCGAGCC AACGGCGCC CCGAATAAT AACATTGAG TACAACCTGT CGAATAGTAG CTATTGAAA TTACGCCATC

Figure 1: Nucleotide and Amino Acid Sequence of the Lamb Signal Sequence and IGF-I (Y24L, Y31A)

[illegible]

FIG. 2

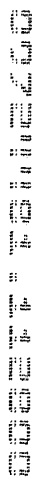


FIGURE 3

plasmid IGFM1
length: 5115 (circular)

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CTTAAGTTGA AGAGATATGA AACCTATTC TTATATCTTG TACTTTTAG AGTACAGACT CAACTAATAA TTGAAACGGG TTTTCTCT TCTACAGTA
101 GAAGTGTG CCGAGTAGA AGCTTGGAG ATTATCTCA CTGCATGCT TCGCATATG GCCCAAAATG ACCAACAGG GTTAAATGAT CAGGTAGAG
CTTGACACAC GCGTCATCT TCGAACTTC TAAATAGAGT GAGCTTACG AGGTTATATC CCGCTTTTAC TGGTGTCC CAACTAATA GTCCATCTCC
201 GGGCGCTGA CAGGTAAAG CCCGATGCC GCAATCTCGA CGACATAGG GAGCTGTC GCGATTACG TTAAGAGTA TTGAACATC CTCTCAGTA
CCCGGACAT GCTCAATTC GGGCTACGGT CGTAAAGACT CCTGCTATG CTGACAGAGC CGCTAATGCA TTTCTCAAT AACTGTAG GACAGTCAT
301 AAAAGTAAT CTTTCAACA GGTGCTATA AGTGTACAG GCCGAGACT ATAGTGGCT TGTTTTAT TTTTAATGA TTGTACTA GTACGAACT
TTTTCATTA GAATGTTCT CGACAGTAT TCAACAGTGC CCGCTCTGA TATACAGGAA ACAAATAA AAATTAAT AACATTGAT CATGCGTTCA
401 TCACGTAAA AGGTATCTA GAATATGAT GATTACTCTG CCGAACTTC CTCTGGGGT TGGCGTCCA GCGGCGTAA TGTCTCTCA GCGCATGGC
AGTCATTTT TCCATATGAT CTTAATGACT CTATAGAGAC GCGTTTGAAG GAGACCGCA ACAGGACGCT CCGCCGCAAT ACAGACGAG CCGGTACCG
1 Methe C11ethIeu ArglyLeuP foleuAlaVa lAlaValAla AlaglyValH eSerAlaG1 nAlaMetAla
501 GTTCCCGAAA CTCTGCGCG TCGTGAAGTG GTTGACGCTC TGCAGTTGCT ATGTGGAT CAGAGGCTTC TGTTCACAA ACCGACTGG GCTGATCT
CGAGGGCTT GAGACAGCG AGGACTGAC CAACTGCGAG ACCTACAGCA TACACCACTA GCTCCGAAAG ACAATTTGT TGGTACCC CCACTAGGA
26 GlyProGluT hIleuCyseI yAlaGluLeu ValAspAlaL eugInPheVa lCySgLyAsp ArgolYPheL eupheAsnly sProthrgly AlaglySerSer
601 CCTCTCGTCG TCGTCCCGAG ACTGATATG TTGACGAATG CTGCTTTGCT TCTTGGAGC TGGCTCGCT GGAATGTAT TCGGCTCCC TGAACCCCG
GAGAGCAGC ACAGGGGCTC TGACCATTAAC AACTGCTTAC GACGAAGA ACAAAGCTGG ACAGACAGCA CCTTACATA ACCGAGGGG ACTTTGGCG
60 SerArgAr gAlaProGln ThrGlyIleV alaSpGluCy sCySphearg SerCyAspL euaArgargle uGluMettyr CyAlaProl euIySProAla
701 TAAATGCT TAGAGCTCC TAAGGCTCGG TTGGCGCGCG GCGTTTTTA TTGTTAATC ATGTTGACA GCTTATCATC CATACCTT AATCGGTAG
ATTAGACGA ATCTTCAGAG ATTGCAGCC AACGGCGCC CCGAAAAAT AACAAATGAG TACAACTGT CGAATATAG CTAATCGAA TTACGCATC
93 LysSerAla Am⁺
801 TTTATCACG TTAATGCT AACGAGTCA GGCACCGCT ATGAATCTA ACAATGCGT CATGCTCATC CTGGACCGG TCACCTGGA TCGTGAAGC
AAATAGTTC AATTACGA TTGCGTCACT CCGTGGCACA TACTTTAGT TGTACGCCA GTACAGTAG GAGCGTGC AGTGGAGCT ACACATCCG
901 ATAGGCTGG TTATGCCGCT ACTGCCGGG CTCTTGGGG ATATGCTCA TTCCGACAGC ATGCCAATC ACTATGGCT GCTGTAAGC CTATATGCT
TATCCGAAC AATAGGCCA TGACGGCCG GAGAACGCC TATACAGT AAGCTGTG TACGGTCA TGAATACGCCA CGACGATCCG GATATACGA
1001 TGATGCAAT TCTATGCCA CCCGTTCTG GAGCACTGTC CGACCGCTT GGGCGCGCG CAGTCTGCT CCGTTCCGTA CTTGAGCCA CTATCGACTA
ACTACGTTA AGATACGCT GGGCAAGAG CTGCTGACG CTGCGGAAA CCGCGCGCG GTCAAGACGA GCGAAGCAT GAACCTCGT GATAGCTGAT
1101 CCGGATCAG GAGACAGAC CCGTCTGTC GATCTCTAC GCCGAGCA TCGTGGCGG CATACCGCG GCGACAGGT GGGTGTGG CCGCTATATC
GCGCTAGTAC CCGTGTGTG GAGAGACAC CTAGGAATG CCGCTGCT AGCACCGCG GTAGTGGCG CCGTCTAC GCCAACAGC CCGCATATAG
1201 GCGGACATCA CCGATGGGA AGATGGGCT CCGCACTTCG GCGTATATG CCGTTTTC GCGTGGGTA TGGTGGCAG CCGCGTGGC GGGGAGATG
CGGCTGATG GGTACCCCT TCTAGCCGA GCGGTGAAG CCGATATCT GCGAACAAAG CCGCACCAT ACACCGTCC GGGGACACCG CCGCTACAA

00201104:442000

FIGURE 3 (cont'd)

1301 TGGGGCCCAT CTCCTGCAT GCACATTCC TTGCGCGCGC GGTGCTCAG GGCCTCAGC TACTACTGGG CTGCTTCCTA ATGCAGAGT CGCATAGAGG
 ACCCGCGGTA GAGGAACGTA CGTGTAGAG AACGCCCGCC CCACAGTTG CCGAGATTGG ATGATGACCC GACGAAGAT TACGTCTCA GCGATTCCG
 1401 AGAGCTCGA CCGATGCCCT TGAGAGCCT CAACCCAGTC AGCTCTTCC GGTGCGCGC GGCATGACT ATCGTGGCG CACTTATGAC TGTCTCTT
 TCTCGAGCT GCGTACGGGA ACTCTGGAA GTTGGGTGAG TCGAGAGAG CCACCCGCGC CCCGTACTGA TAGACCGGC GTGAATACTG ACAGAGAAA
 1501 ATCATGCAGC TCGTAGACA GGTGCCGCGA GCGCTCTGGG TCATTTCGG CGAGAGCCG TTTCGCTGA GCGGAGAT GATCGGCTG TCGCTTGGG
 TAGTACGTTG AGCATCCTGT CCACGGCCGT CCGGAGACCC AGTAAAGCC GCTCTTGGCG AAGCCAGCT CCGCTGCTA CTAGCCGAG AGCGAACCC
 1601 TATTGGAAAT CTTCACGCC CTGCTCAGG CTTCTGTAC TGTCCCGCC ACCAACTT TCGCGAGA GAGGCCAT ATGCCCGCA TGGCGCGGA
 ATMACCCTA GACGTGCGG GAGCGAGTTC GGAACAGTG ACCAGGCGG TGGTTGCA AGCCGCTCTT CGTCCGTA TACGGGCGT ACCGCGGCT
 1701 CCGCTGGG TACGTCTGC TGGCTTCC GACCGAGCC TGGATGCC TCCCATTA GATTCTTC GCTTCCGCG GCATCGGAT GCGCGGTTG
 GCGCACCAG ATGCAGAGC ACCCGAACG CTGCGCTCCG ACCTACCGGA AGGGTAATA CTAGAGAG CGAAGGCCG GTAGCCCTA CCGCGCGAAC
 1801 CAGGCCATG TGTCCAGGCA GGTAGATGAC GACCATCAG GACAGTTCA AGAATCGTC GCGGCTTA CCAGCTTAC TTGATCACT GAACCGTGA
 GTCCGTTAG ACAGTCCGT CCATCTACTG CTGTAATGC CTGTCAAGT TCTTAGCAG CGCCAGAAI GGTGGATTG AACCTATGA CTTGGGACT
 1901 TCGTCAGGC GATTATGCC GCTTCGCGCA GCACATGGA CCGGTTGGCA TGAATGTAG GCGCGCCCT ATACCTTGC TGCCTCCCG CGTTCGCTG
 AGCATGCGG CTAAATACG CGAGCCGCT CGTATACCT GCCCAACCT ACCTAACATC GCGCGGGGA TATGAAAG ACAGAGGGG GAAACGAGC
 2001 CCGTCATG AGCCGGGCA CTTCGACCTG AATGAMGC GCGCGGCTA CGCTAACGGA TTCACACTC CAAGATTG AGCCATCA TTCTTGGGA
 GCCAGTACC TCGGCCCGGT GAGCTGAGC TTACCTCG CCGCCGTA GCGATTGCT AAGTGGTAG GTTCTTACC TCGGTAGT AAGAACGCT
 2101 GAATGTGAA TCGGCAACC AACCTTGGC AGACATATC CATCGCTCC GCCATTCCA GCAGCCGAC GCGCGCATC TCGGCAAGG TTGGTCTG
 CTTGACACT ACCGTTGG TTGCAACCG TCTGTATG GTAGCGAG CCGTAGAGT GGTGCGCTG CCGCGCTAG AGCCGCTG AACCGAGC
 2201 GCCAGGGTG CCGATATCG TGTCTCTTC GTTAGAGC CCGCTAGCT GCGCGGTTG CCTTACTGT TAGCAAGAT AATCACCAT ACCGAGCA
 CCGTCCGAC GCGTACTAG ACAGAGAGC CAACTCTCG GCGATCCA CCGGCCAAC GAAATGACA ATGCTTAC TTAGTGCTA TGGCTGCT
 2301 ACGTGAGG ACTGCTCTG CAAGAGCTT GCGACTGAG CAACATATG AATGCTTTC GGTTCGCTG TTTCGTAA TGTGAAAG CGAAGTCA
 TGCATTCCG TACAGACGAC GTTTGCA GACTGACTG GTTGTATC TTACCAAG AGCAAGGAC AAGCATTC AGACTTTC GCTTCACTG
 2401 CCGCTGAC CATTATGTC CGATCTGA TCGAGATG CTGCTGCTA CCTGTGGA CACTTACATC TGTATTAG AACGCTGC ATTGACCTG
 GCGGAGCTG GTAAATACAG GCTTAGACT AGCTCTTAC GAGACCGAT GGAACACTT GTGATGTAG ACAAATTC TTGCGAGCG TAACGTGAC
 2501 AGTATTTT CTCTGTCC GCGCATCA TACCGCAGT TGTTACCT CACAAGTTC CAGTACCG GCATGTAT CATCAGTAC CCGTATCTG
 TCACTAAA GAGACAGAG GCGGTAGT ATGGGCTCA ACAAATGGA GTGTGCAAG GTCATGGCC CGTACAGTA GTAGCATG GCAATGAC
 2601 AGCATCCTCT CTCGTTTAT CCGTATCAT ACCCCATGA ACAGAAATC CCCCTTAC GAGGATCA AGTACCAA CAGAAAAA CCGCCTTA
 TCGTAGAGA GAGCAAGTA GCCATATGA TGGGGTACT TGTCTTAG GGGGATGTG CCTCCGAT TCACTGTT GTCTTTT GCGGGAAT
 2701 CATGCCCC TTATCAGAA GCCAGACTT AAGCTTCTG GAGAACTCA AGAGCTGA CCGGATGAA CAGCAGACA TCTGTGATC GTTACGAC
 GTACCGGCG AATATGCTT CCGTCTGTA TTGCGAAGC CTCTTGAAG TGTCTGACT GCGCTTACT GTCCGTCT AGACACTT AGAAGTCTG
 2801 CACGCTGAT AGCTTATCG CAGTGCCTC GCGGTTTC GTATGACG TGAAACTTC TGACATGC AGCTCCGGA GACGTACA GCTTGTCTG
 GTGCACTAC TCAAAATGG GTGACGAG CCGCAAGC CACTACTGC ACTTTGAG ACTGTAGC TCGAGGGCT CTGCAAGT CAAACAGACA
 2901 AAGCGATG CCGGAGACA CAAGCCGCT AGGCGGCTG AGCGGCTG GCGGCGAG CATGACCG TCACTAGG ATAGGGAGT
 TTGCTTAC GCGCTCTCT GTTGGGAG TCCCGGAG TCCGCCACA CCGCCACAG CCCGCTCG GTACTGGGT AGTCACTGC TATGCTCTA

FIGURE 3 (cont'd)

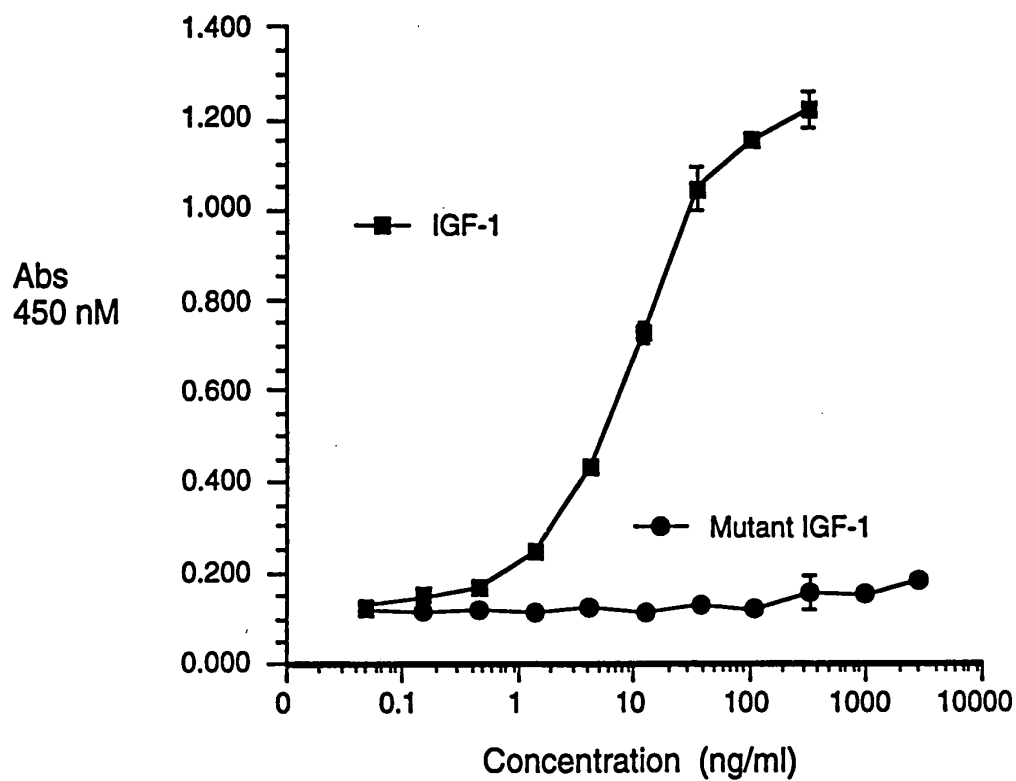
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 CATATGACCG AATGATATAG CCGTACTCTC GTCTAAATATG ACTTCACCT GGTATAGGCC ACACTTATG GCGTGTCTAC GCATTCTCTT TTATAGCGGT
 3101 TCAGGGCGCT TTCCGCTTCC TCGCTACTG ACTCGCTGCG CTCGCTCGT CCGCTCGCG GAGCGTATC AGCTACATCA AAGCGGTAA TACGGTATC
 AGTCCGGCAG AAGCGAAGG AGCGAGTAC TGAGCGAGCG GAGCCAGCAA GCCAGACCGC CTCGCCATAG TCGAGTGAAT TTCGCCATT ATCCAAATAG
 3201 CACAGATCA GGGATATAG CAGAAAGAA CATGTAGCA AAAGGCCAG AAAAGGCCAG GAAACCGTAA AAGCGCGCT TCGTGGCTT TTTCATAGG
 GTGTCTTAGT CCCCTATTGC GTCTTTCTT GTACACTCGT TTTCGGTGC TTTTCGGCT CTCGGCATTT TTCGGCGCA ACGACCGCAA AAGGTATTC
 3301 CTCGGCCCC CTGACGAGA TCACAAAAT CGAGCTCAA GTACAGGTG GCGAAACCG ACAGACTAT AAAGTACCA GCGGTTCCT CCGTGAAGT
 GAGCGGGGGG GACTGCTCT AGTGTTTTAA GCTGCGAGT CAGTCTCAC CCGTTTGGC TGTCTGATA TTTCTATGCT CCGCAAAAGG GAACTTCGA
 3401 CCCTCGTGCG CTCCTCTGTT CCGACCTGCG CCGTTACCGG ATACTGTGC GCCTTCTCC CTCGGGAG GCGCGCGTT TCTCATAGCT CACGCTGAG
 GGGAGCACGC GAGAGACAA GCGTGGGAG CCGAATGGCC TATGACAAAG CCGAAAGAG GAAACCTTC GCACGCCAA AAGTATCGA GTCCGACATC
 3501 GATCTCAGT TCGGTGTAGG TCGTTCGCT CCACTGGCAG TGTGTGACG AACCCCGCT TCAGCCCGAC CCGTGGCTT TATCCGTTA CTATCGTTA
 CATAGAGTCA AGCCACATCC AGCAAGCAG GTTCGACCCG ACACAGTGC TTGGGGGCGA AGTCGGGCTG GCGACGGCGA ATAAGCCATT GATAGCGAA
 3601 GAGTCMAAC CGGTAAAGCA CGACTATTC CCACTGGCAG CAGCCATGG TAAACAGATT ACAGAGCGA GGTATGTAGG CCGTGTACA GACTCTTGA
 CTCAGGTGG GCCATTCTGT GGTGAATAGC GGTGACCGTC GTCGGTGACC ATGTCTTAA TCGTCTCGT CCAATACATC GCCACGATG CTCMAAGAT
 3701 AGTCGTGGC TAACTAGCG TAACTAGAA GGAAGTATT TGGTATCTG GCTGTCTGA AGCCAGTTAC CTTCGGAATA AAGTTGGTA GCTCTTATC
 TCACCAACCGG ATTGATGCGG ATGTATCTT CCTGTCTATA ACCATAGAGC CGAGACACT TCGGTCAATG GAAACCTTT TCTCAACAT CGAAGACTAG
 3801 CGGCAAGCA ACCACCGCT GTAGCGGTG TTTTCTGT TCGAAGCAG AGATTAGCG CAGAAATAA GAATCTAAG AGATCTTT GATCTTTCT
 GCCCTTGTG TGTGCGCGAC CATCGCAC AAAAACAACA ACCTTCGTC TCTAATGCC GCTTTTTTT CCTAGATTC TTCTAGAAA CTGAAAGA
 3901 ACGGGGTG AGCTCAGTG GAACGAAC TCAGCTTAG GGAATTTGT CATGAGTTA TCAAAAGCA TCTTCACTA GATCTTTA AATTAATAT
 TCGCCAGAC TCGAGTAC CTGCTTTG AGTCMAATC CCTAACAAC GATCTAAT AGTTTTCTT AAGATGAT CTAGAAAT TTAATTTTA
 4001 GAAGTTTAA ATCAATCTAA AGTATATAG AGTAACTTG GTCTGACAT TACCAATCT TAAATCAGTA GGCACCTATC TCAGCAATC GTCTATTCG
 CTTCAAAAT TAGTTAGATT TCAATATATC TCAATTTGAC CAGACTGTA ATGTTAGCA ATTAGTACT CCGTGGATAG AGTCGTAGA CAGTAAAGC
 4101 TTCAATCATA GTTGCCTGAC TCCCGCTCT GTAGATACT ACAGTAGGG AGGCTTACC ATCTGGCCC AGTCTGCAA TGAATCCGG AGACCAACG
 AAGTAGGTAT CAACGACTG AGGGCGACGA CATCTATTGA TGCTATGCC TCCGAAATG TAGACCGGG TCACGACGT ACTATGGCG TCTGGGTGCG
 4201 TCACGGGCTC CAGATTATC AGCAATTAAC CAGCCAGCG GAAAGCCGA GCCAGAAAT GGTCTGCAA CTTATCCG CTCATCCAG TCTATTAT
 AGTGGCCGAG GTCTAAATAG TCGTTATTTG GTCGTCTGCG CTTCGGCT CCGCTTCA CAGAGACGTT GAATAGCGG GAGTAGTIC AGATTAATTA
 4301 GTGCGCGGGA AGCTAGATA AGTATTCGG CAGTAAATAG TTTGGCAG GTTGTGCCA TTGCTGAGG CATCTGTG TCACGCTCGT CGTTGGTAT
 CAACGGCCCT TCGATCTCAT TCAATCAAGG GTCAATATC AAACGGGTG CAACACGGT AACGACGTG GTAGCACAC AGTGGAGCA GCAAAACATA
 4401 GCGTTCAATC AGCTCGGCT CCCAAGATC AAGCGAGT ACATGATCC CCAATGTGT CAAAAAGCG GTTAGCTCT TCGGTCTCC GATGCTGTC
 CCGAAGTATG TCGAGGCCAA GGGTGTCTAG TTCCGCTCAA TGTACTAGGG GGTAAACAC GTTTTTCC CAAATCAGGA AGCCAGAGG CTACACAG
 4501 AGAAGTAACT TGGCCCGAG GTATCACTC ATGGTTATG CAGCACTGA TAAATCTCT ACTGTATC CATCCGTAAG ATGCTTTCT GTAGCTGAT
 TCTTCAATCA ACCGGGCTCA CAATAGTAG TACCAATAC GTCTGACGT ATTAAGAGA TGACAGTAG GTAGGCAATC TACGAAAGA CACTGACAC
 4601 AGTACTCAC CAGTCAATC TGAGATAGT GTATCGGCG ACCGAGTGC TCTTGGCCG GGTCAACAG GATTAATAC GCGCCACATA GCAGAAAT
 TCATAGGTG GTTCAATAG ACTCTATCA CATACGCCG TGGCTAAGG AGAAGGGCC CAGTTGTGC CCAATATAG CCGGCTGAT GGTCTGAAA

FIGURE 3 (cont'd)

4701 AAAGTGTC ATCATTGGA AACGTCCTC GGGGGGAAA CTCTGAAGA TCTACGGCT GTTGAGATCC AGTCGATGT AACCCACTCG TGCACCCAAC
 TTTTCACGNG TAGTAACCTT TTGCAGAGAG CCCCCTTTT GAGAGTTCCT AGAATGGCGA CACTCTAGG TCAAGCTACA TTGGGTGAG ACGTGGGTG
 4801 TGATCTTCAG CACTTTTAC TTTCACCAGC GTTCTGGGT GAGCAAAAC AGGAAGCGA ANTCCCGAA AAAAGGAAT AAGGGCGCA CGGAATGTT
 ACTAGAGTC GTAGAAATG AAGTGGTCG CAAGACCA CTCGTTTTG TCCCTCCGT TTACGGCGT TTTCCCTTA TTCCCGCTGT GCCTTACAA
 4901 GAATACTCAT ACTCTTCCT TTCAATATT ATTGAAGCAT TTATCAGGT TATGTCTCA TGAGCGATA CATATTGAA TGTATTAGA AAAATTAACA
 CTTATGAGTA TGAAGGAA AAGTTATA TAACCTCGTA AATAGTCCA ATAACAGAT ACTGCCAT ATATTAACCTT ACATAAATCT TTTTATTGT
 5001 AATAGGGGT CCGCGACAT TTCCCGGAA AGTGCACCT GAGCTTAG AACCATTA TATCATGACA TTAACCTATA AAAATAGCG TATCAGAG
 TTATCCCAA GCGCGGTGA AAGGGCTTT TCACGTGGA CTGCAATTC TTGTGTAATA ATAGTACTGT AATGGAAT TTTTATCCG ATAGCTCC
 5101 CCCTTGTC TCAG
 GGAAGCAG AAGT

FIG. 4

IGF-1 KIRA in Human MCF-7 Cells
Comparison of IGF-1 and Mutant IGF-1



IGF-1 (Leu²⁴ Ala³¹) is Inactive In Vitro

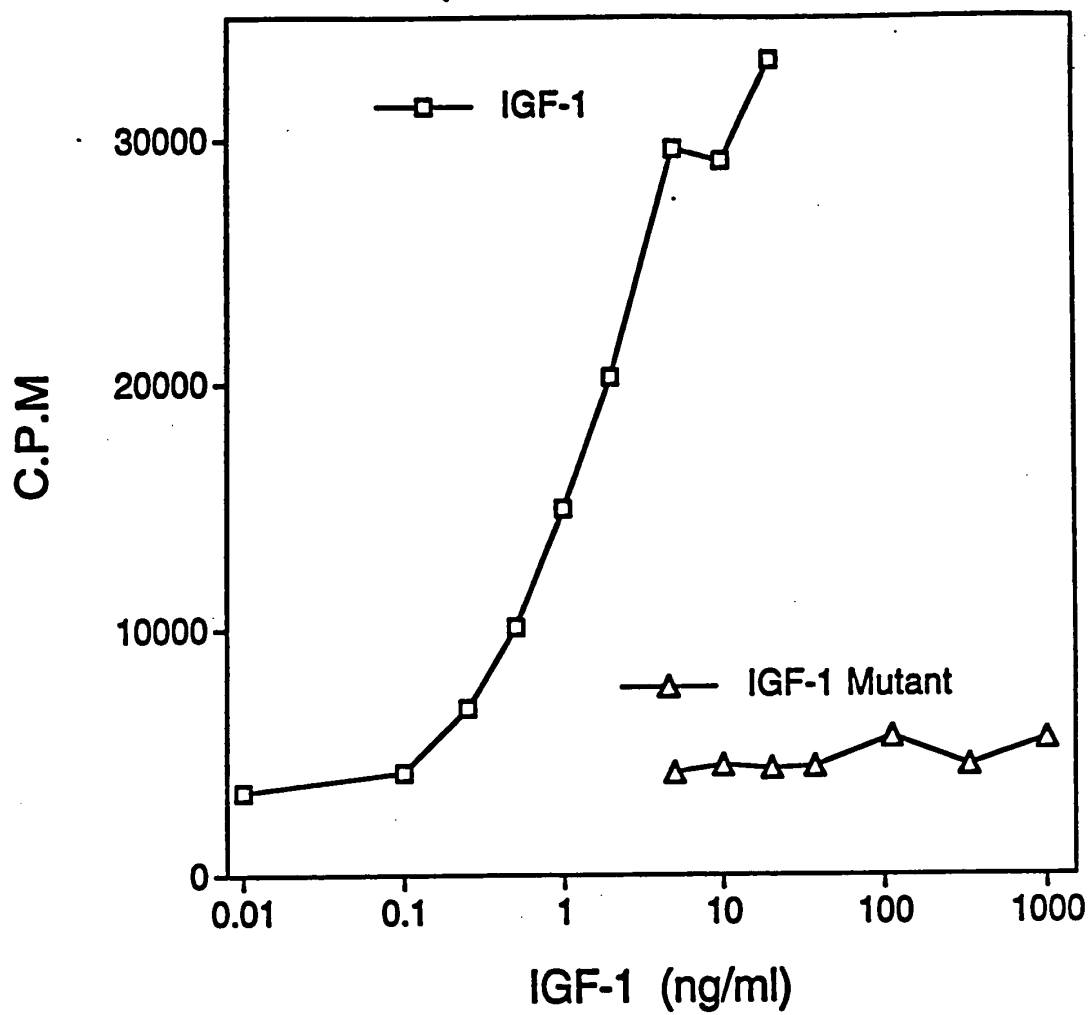


FIG. 6

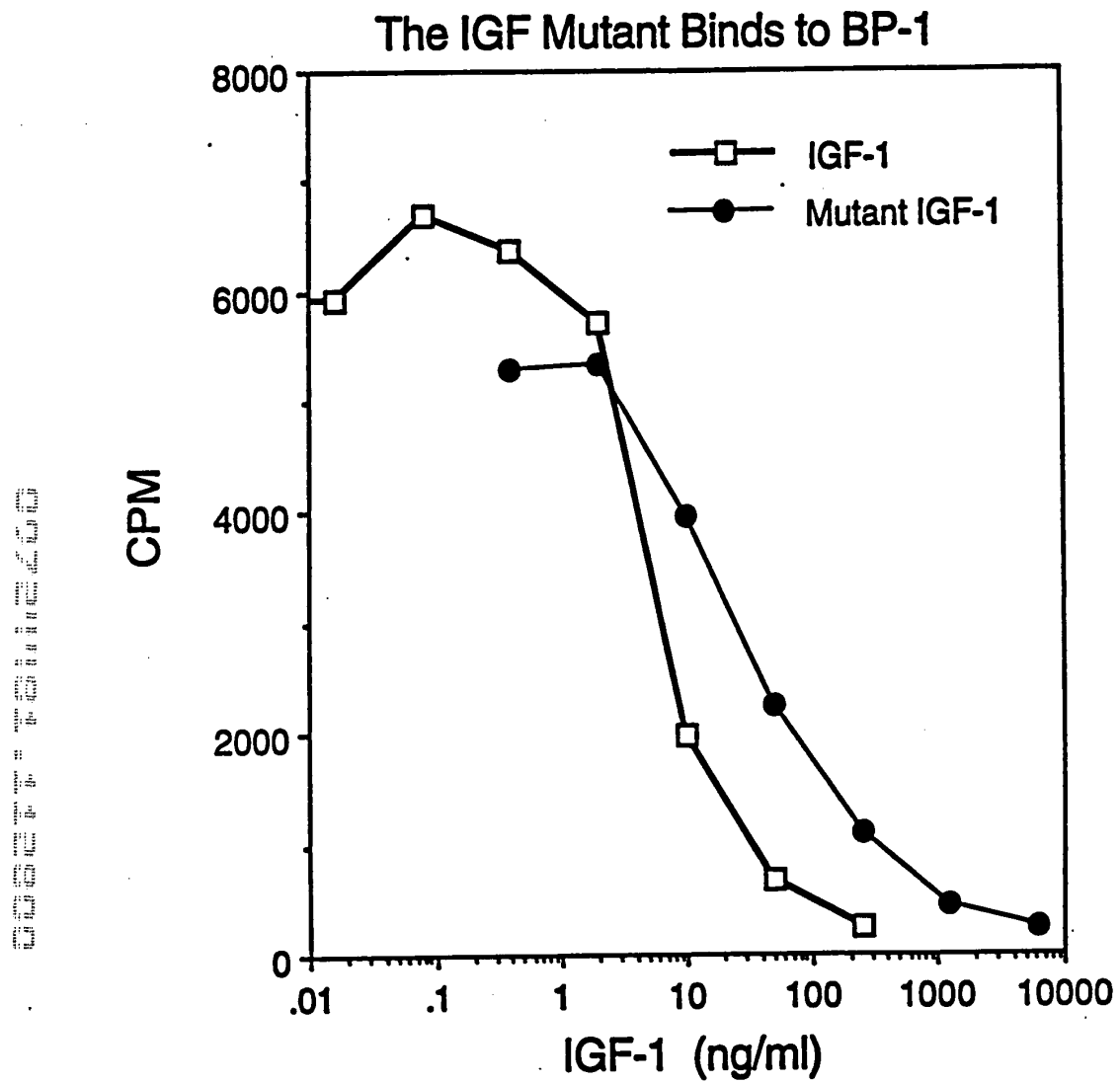


FIG. 7

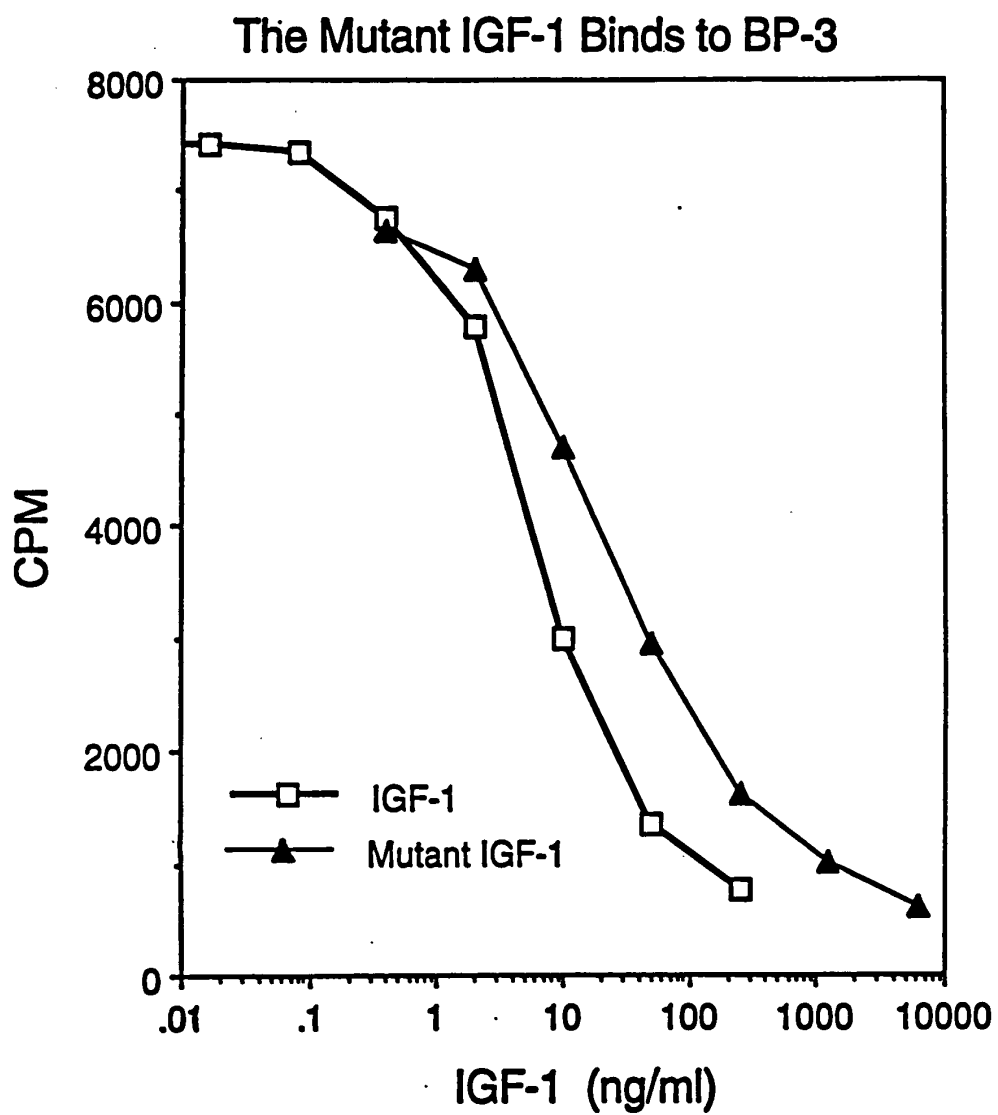


FIG. 8

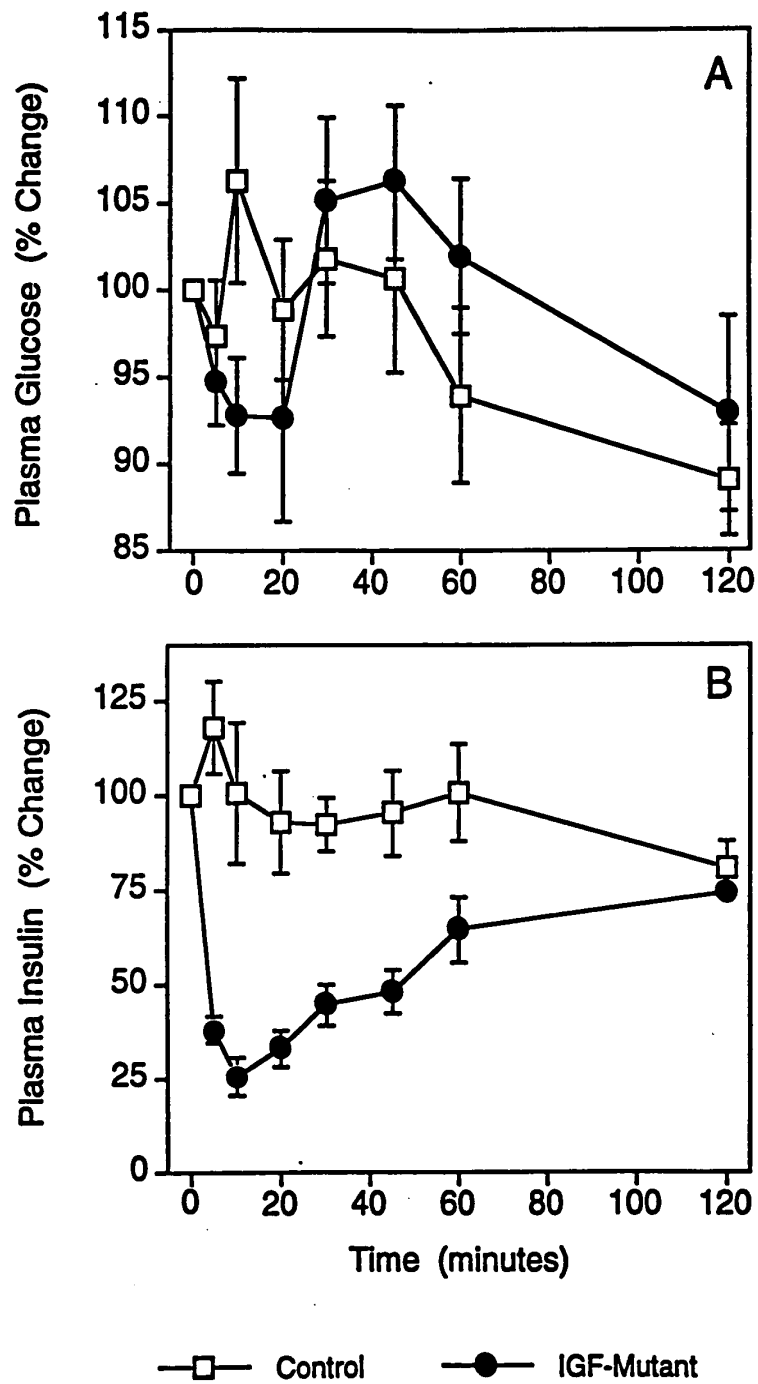


FIG. 9

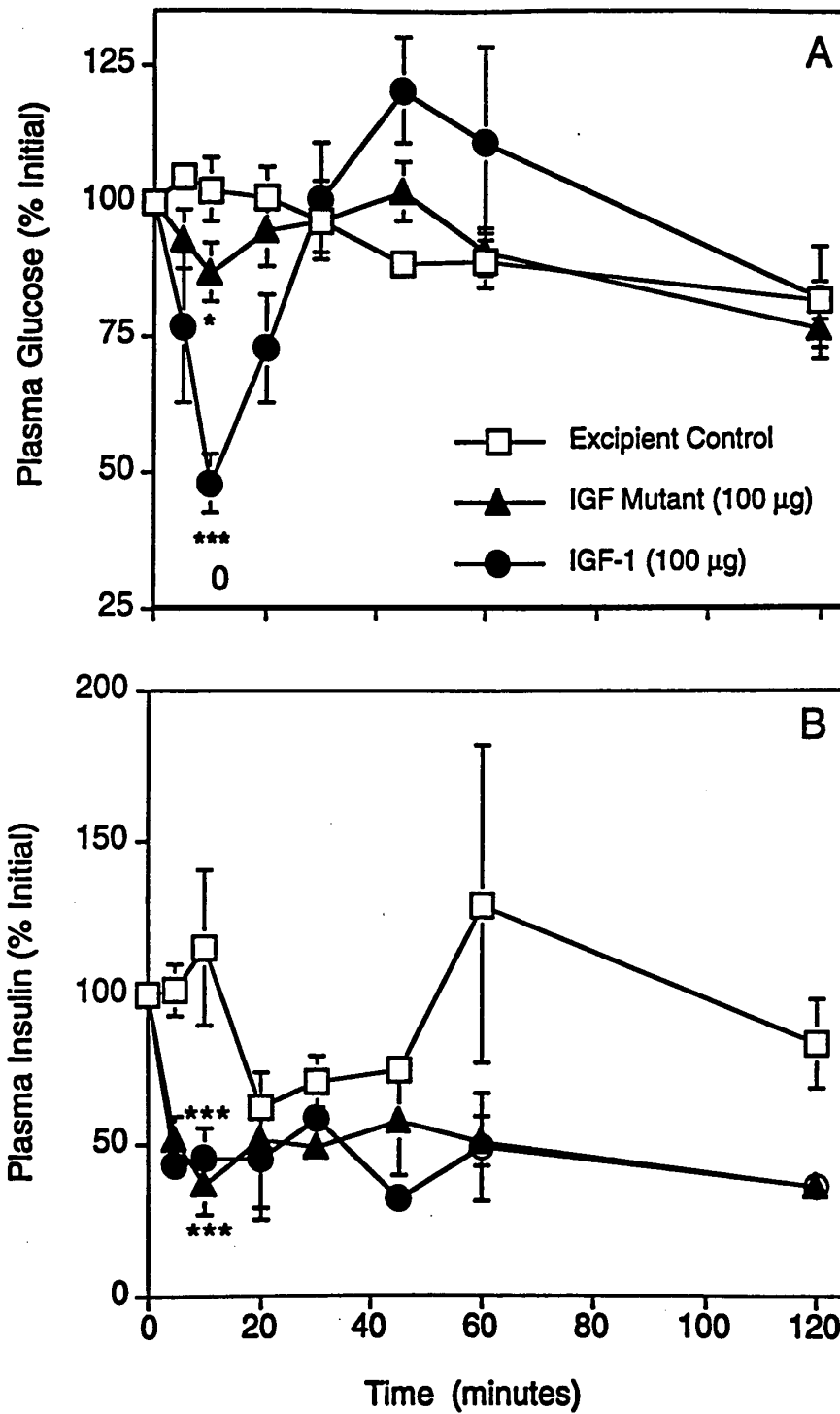


Figure 10

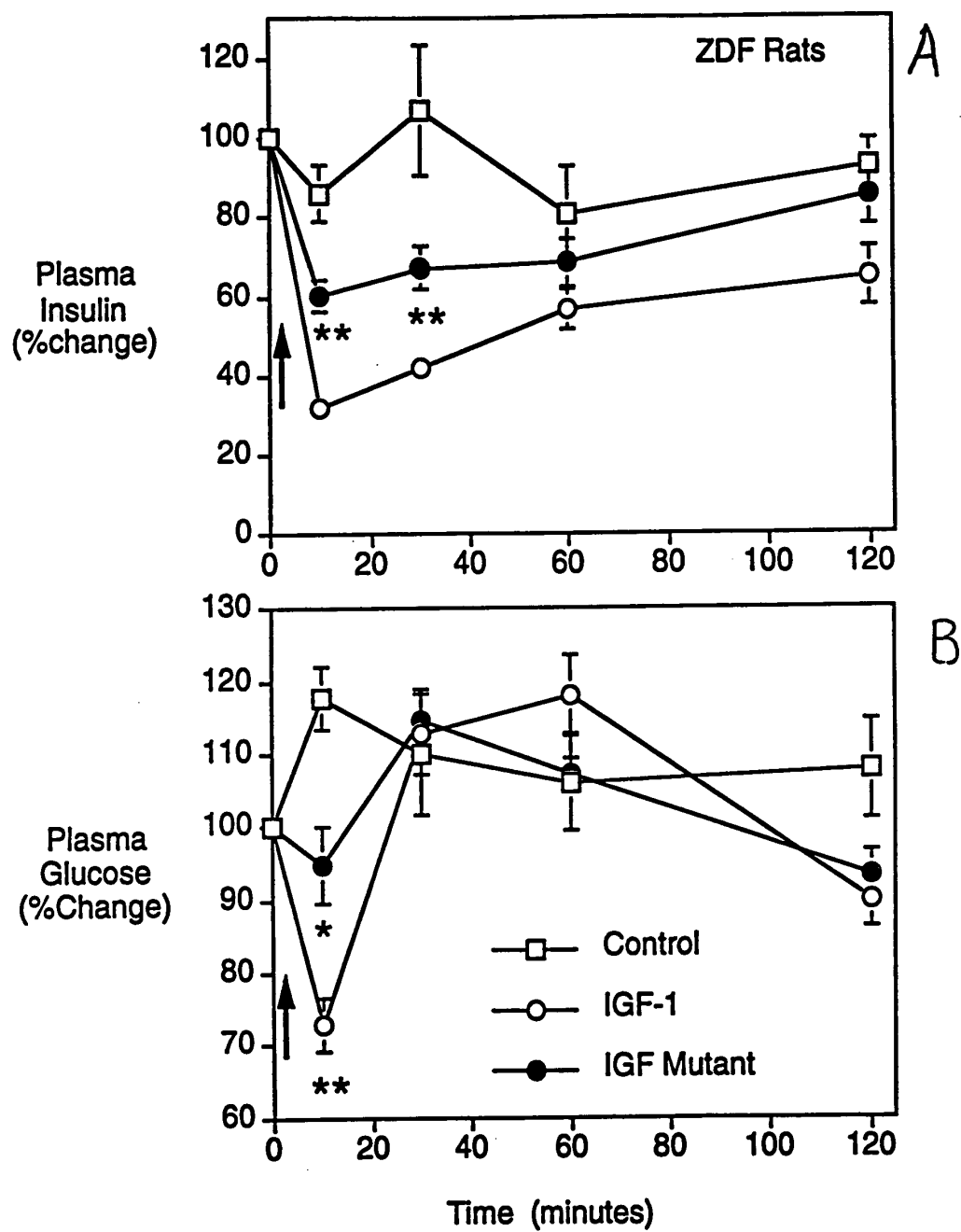


FIG. 11

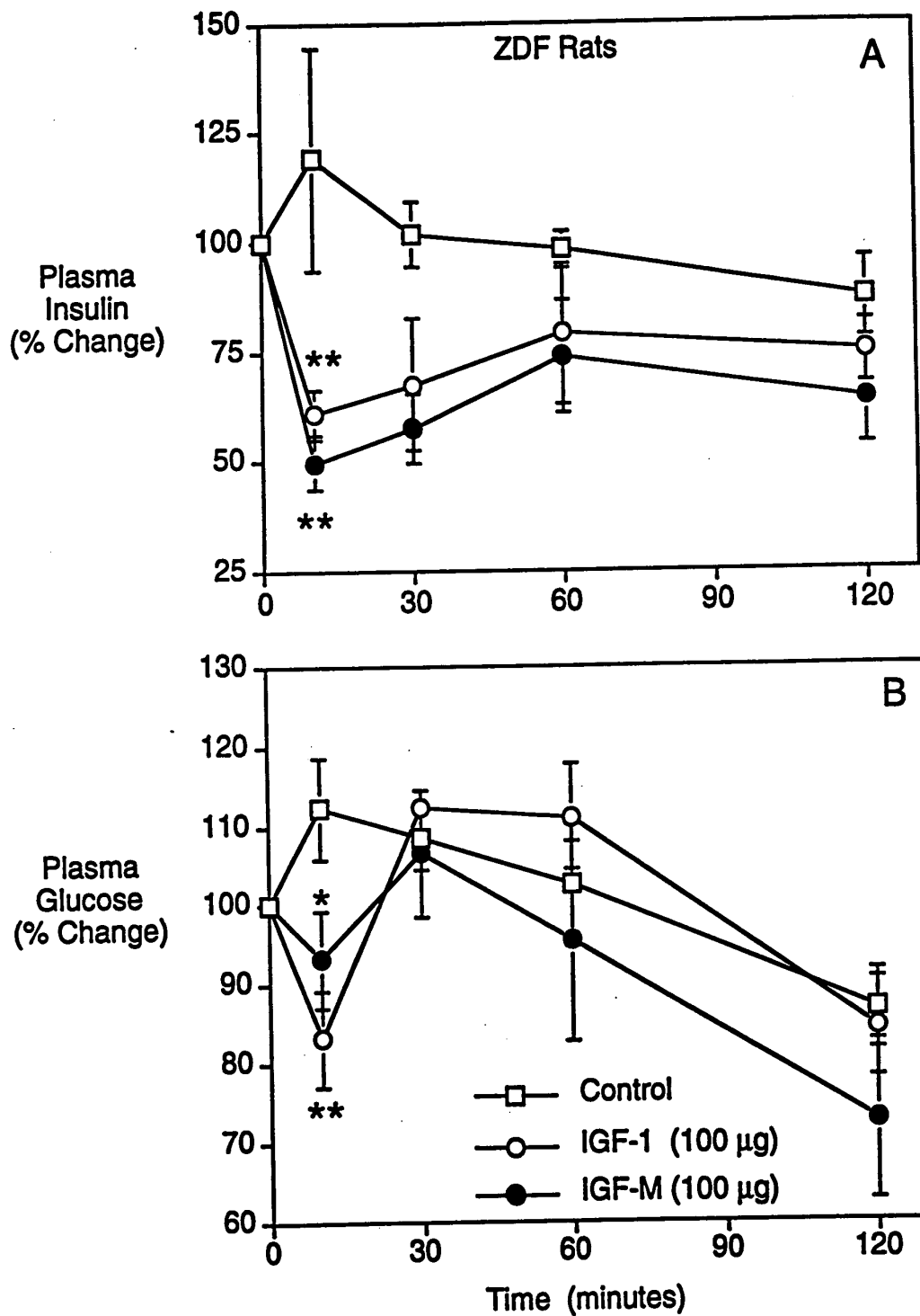


FIG. 12

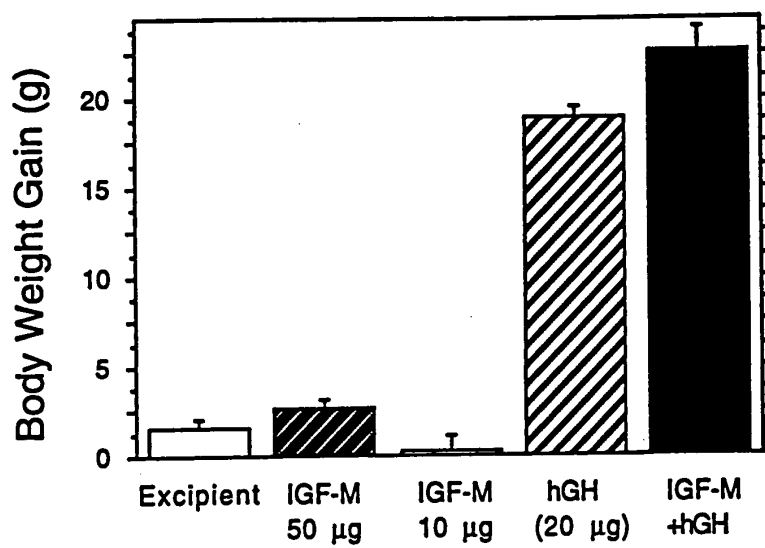


FIG. 13

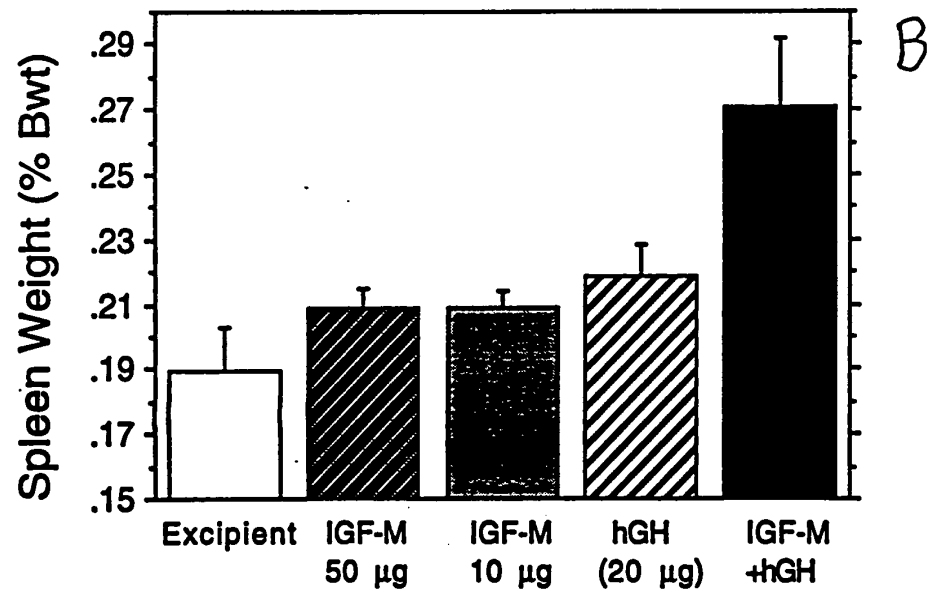
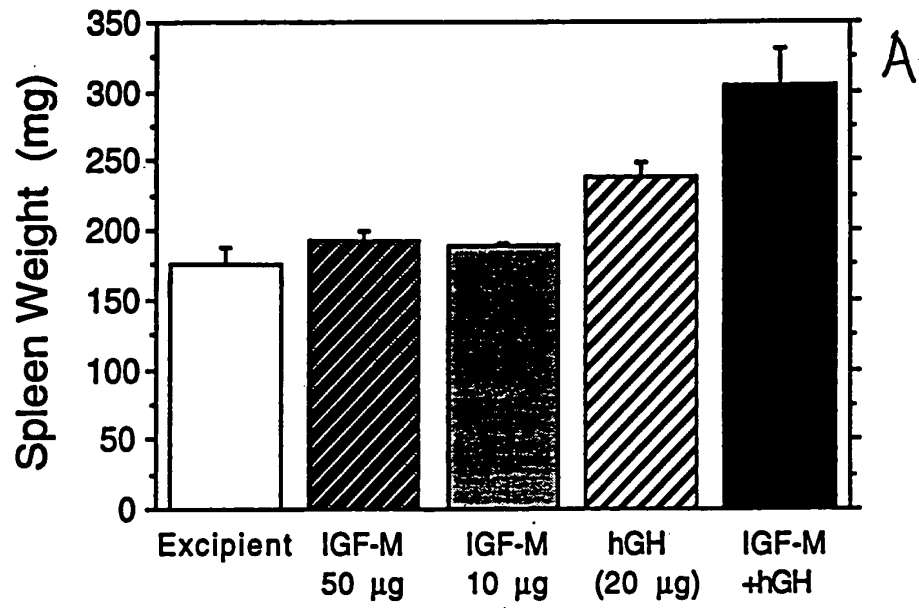
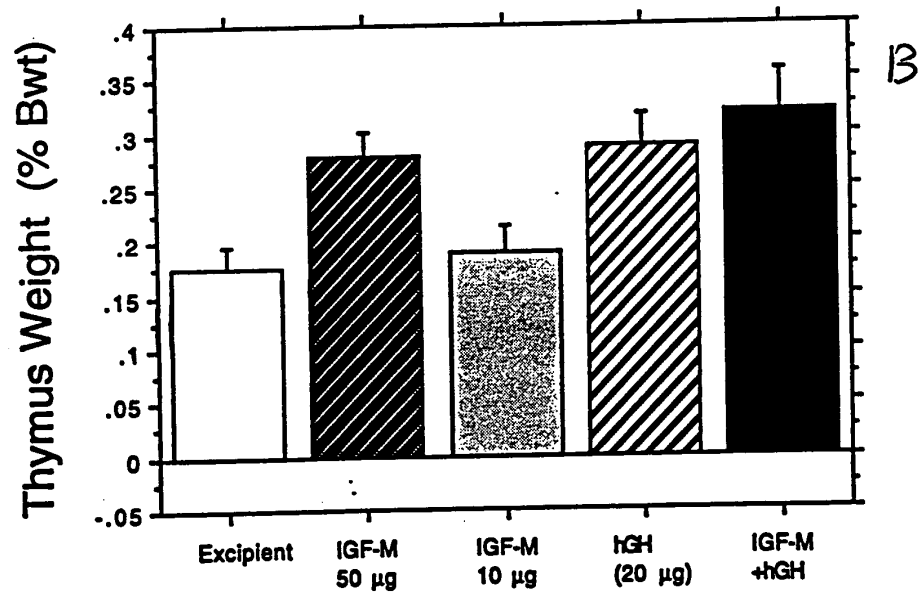
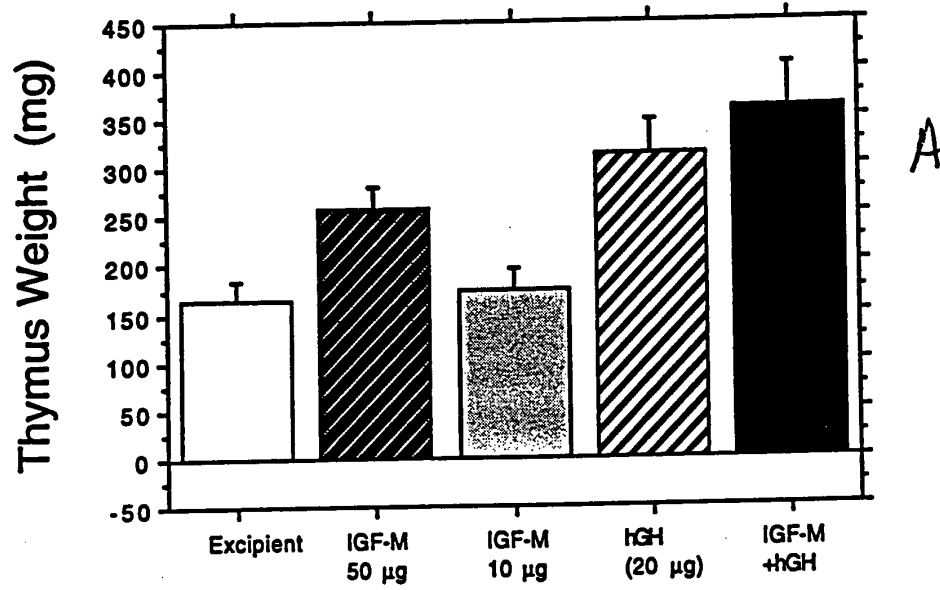


FIG. 14



000007-00000000

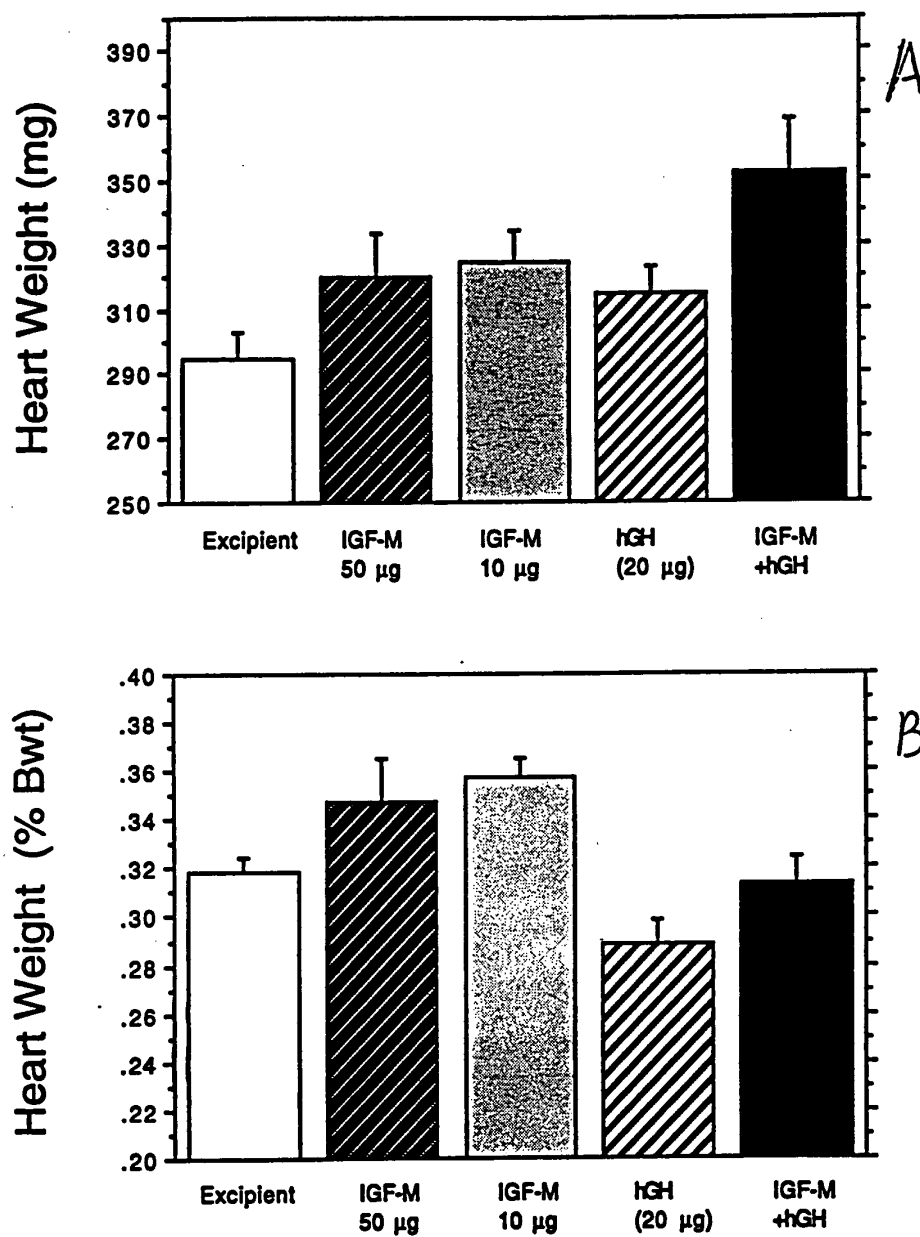
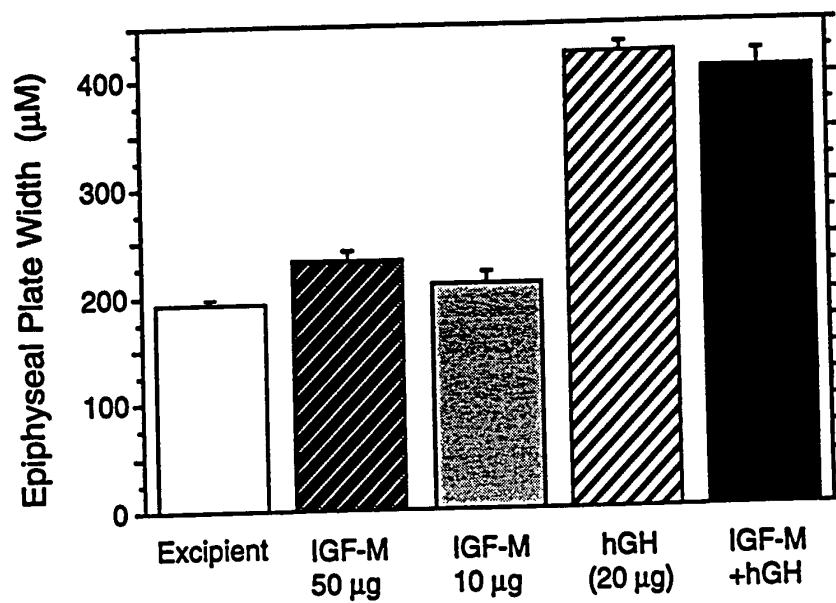


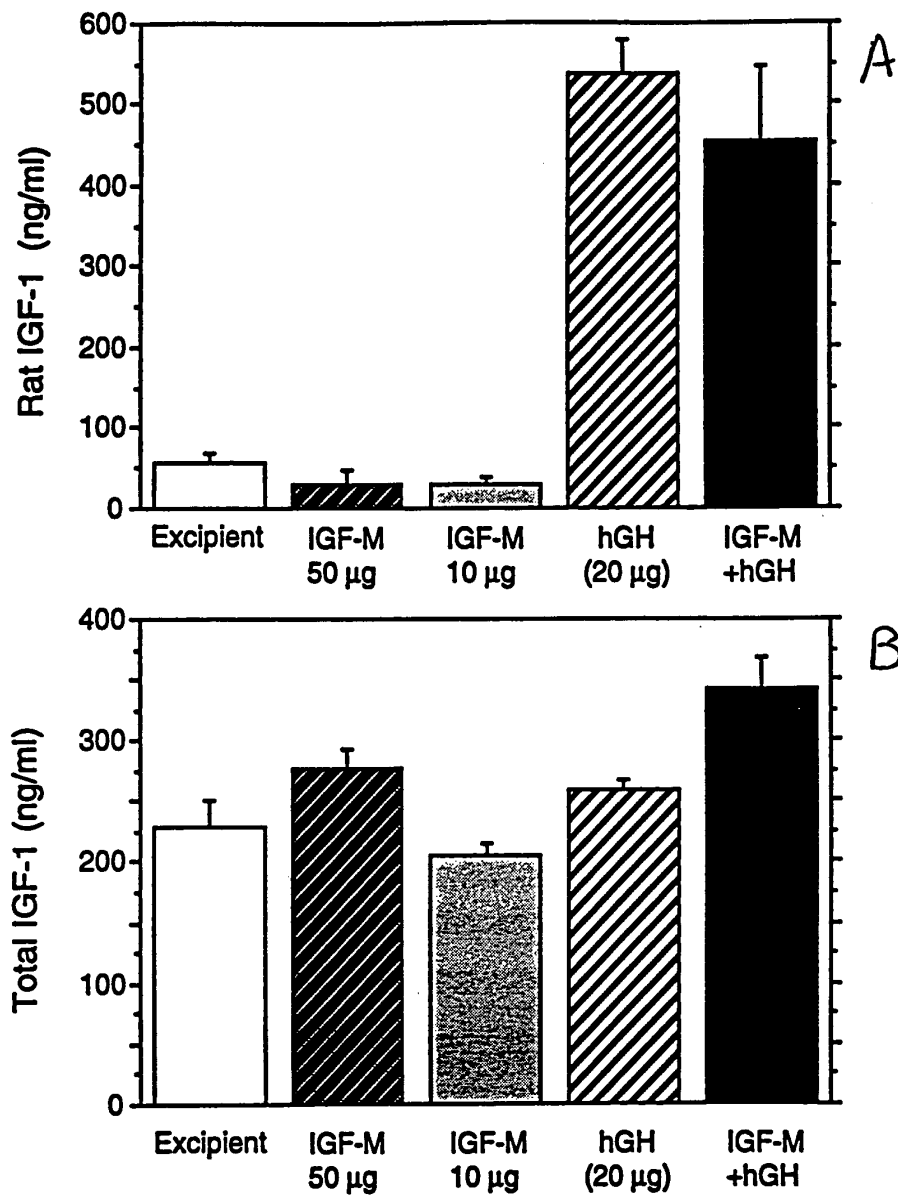
FIG. 15

FIG. 16



20000777 20110220

FIG. 17



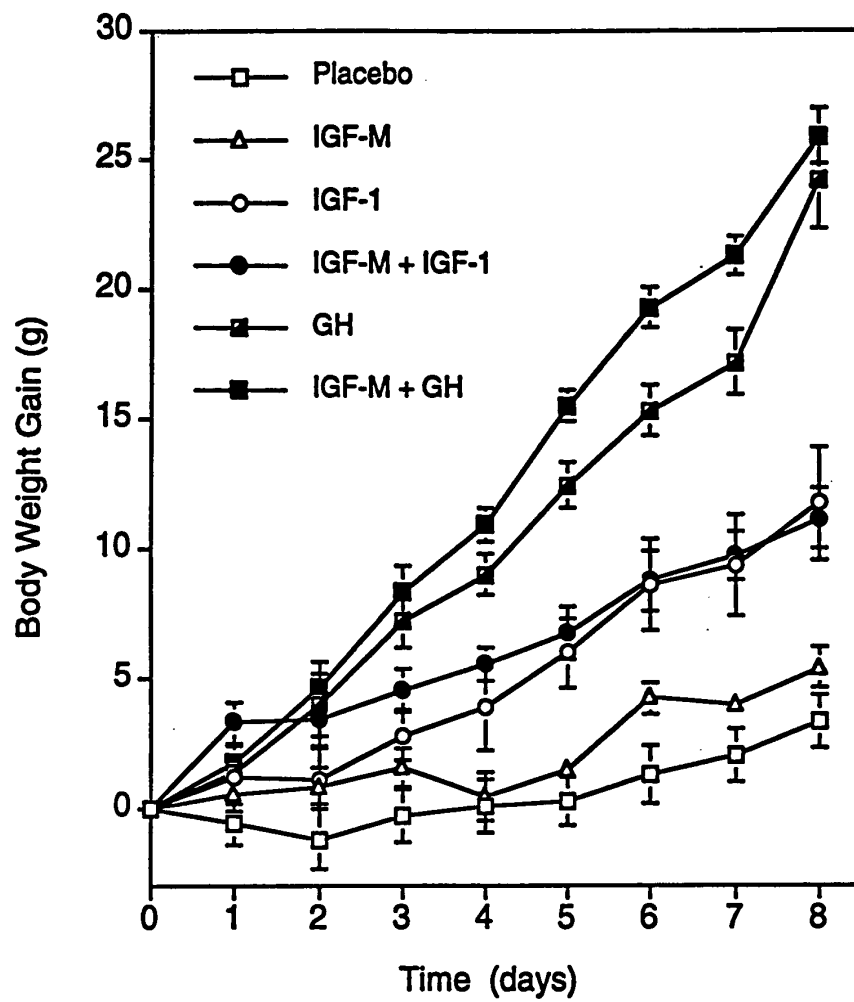


FIG. 19

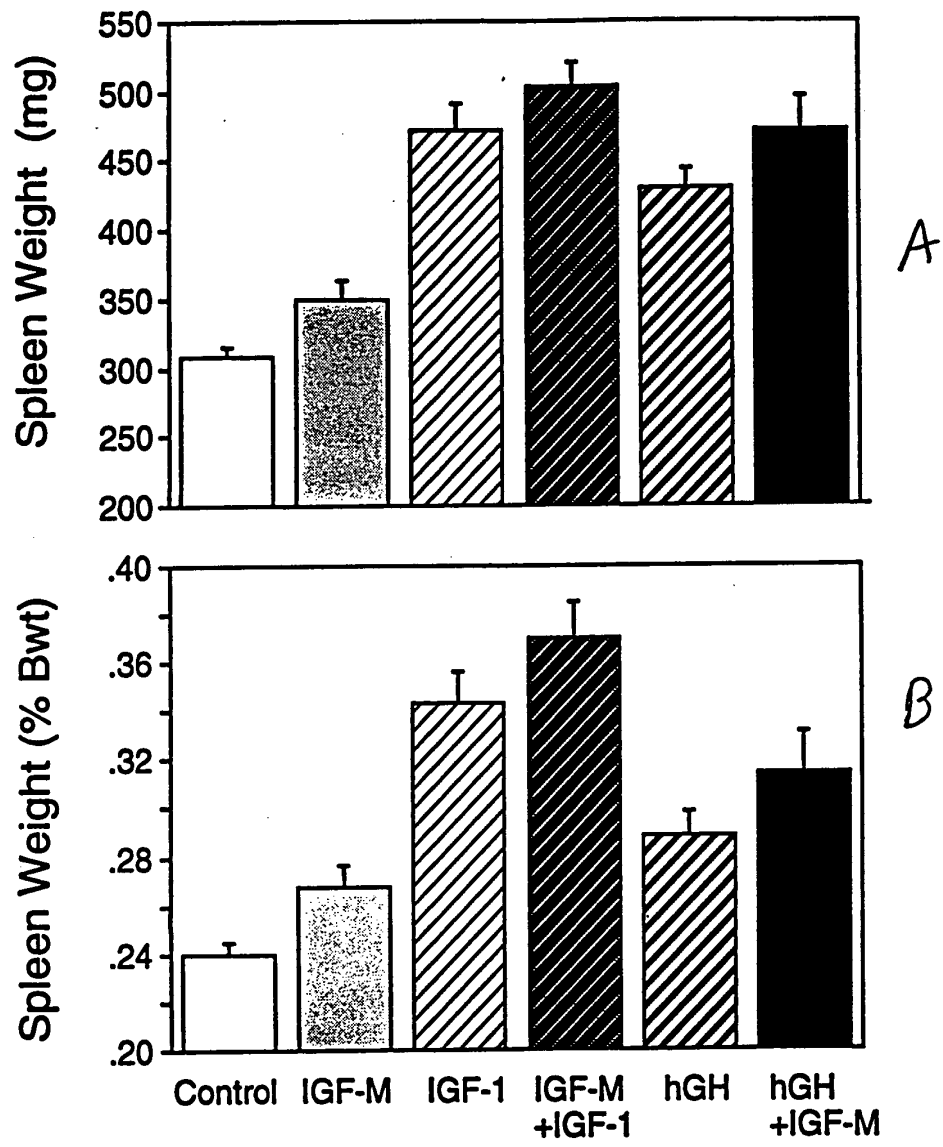


FIG. 20

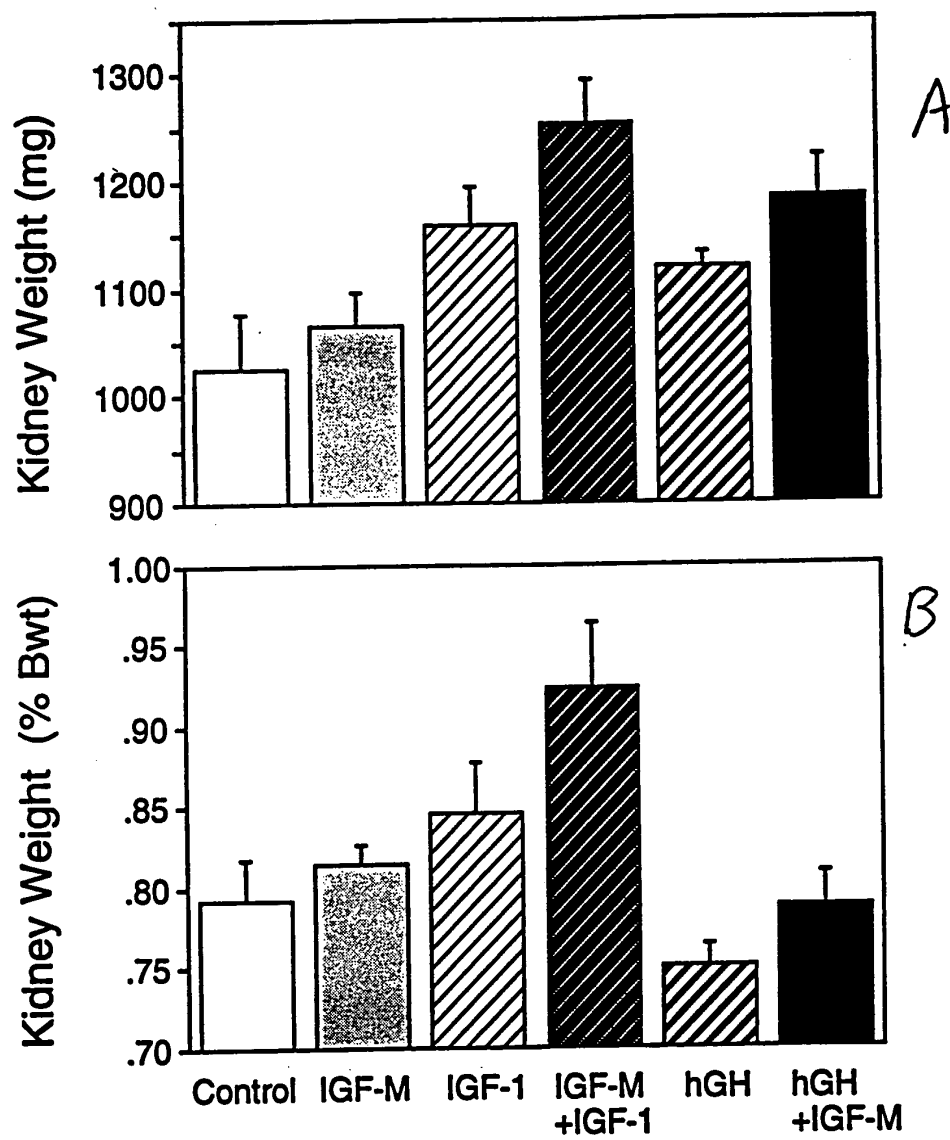
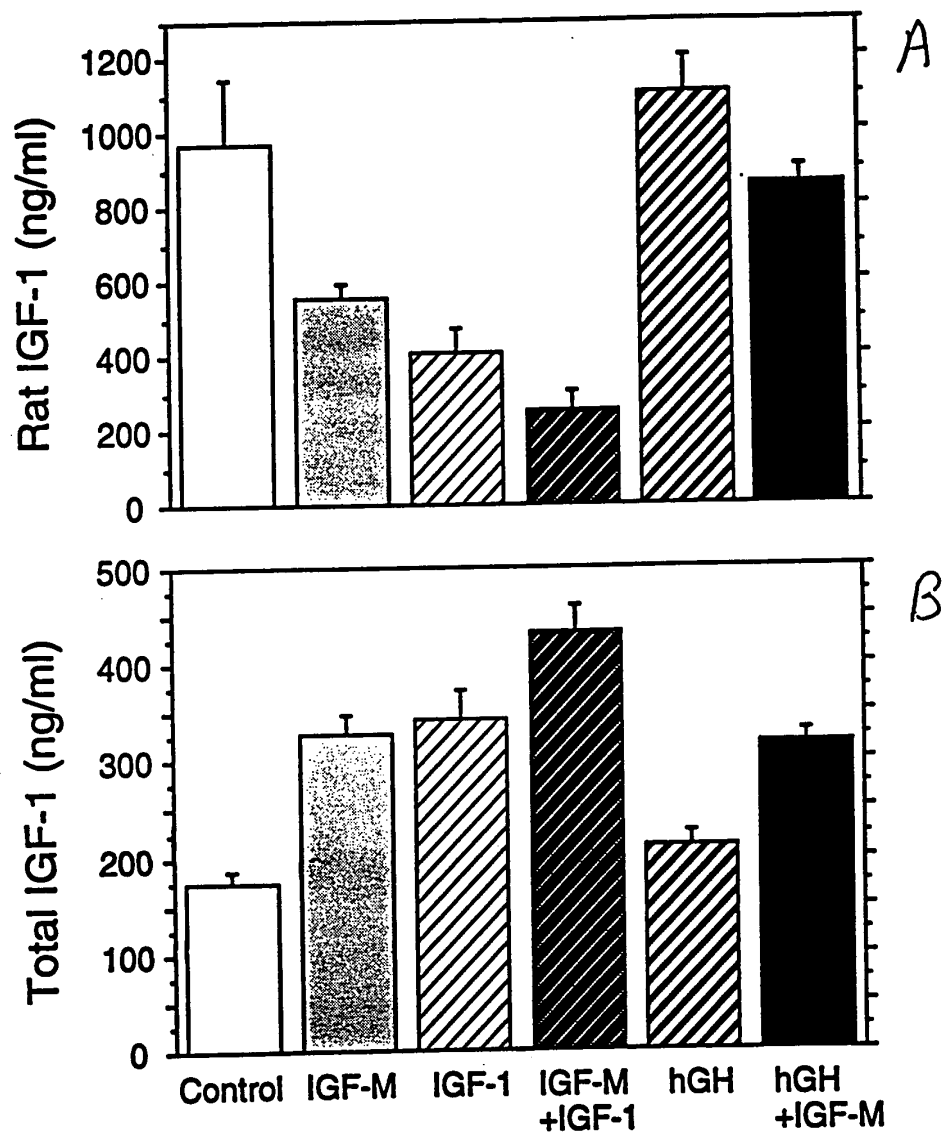
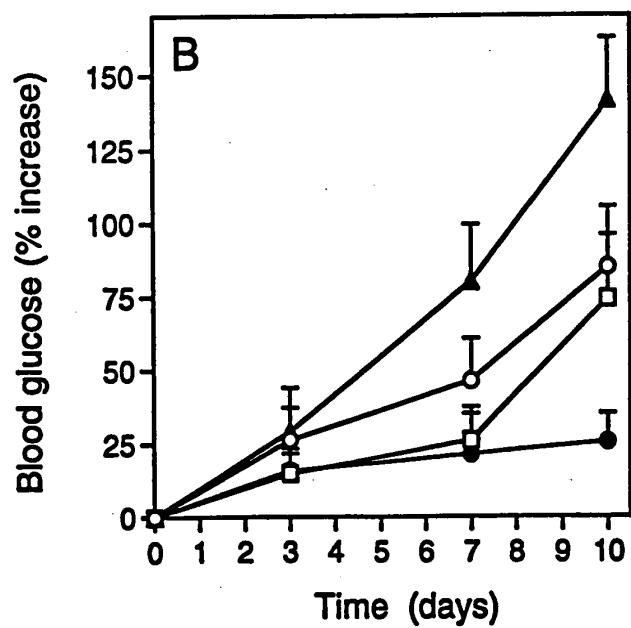
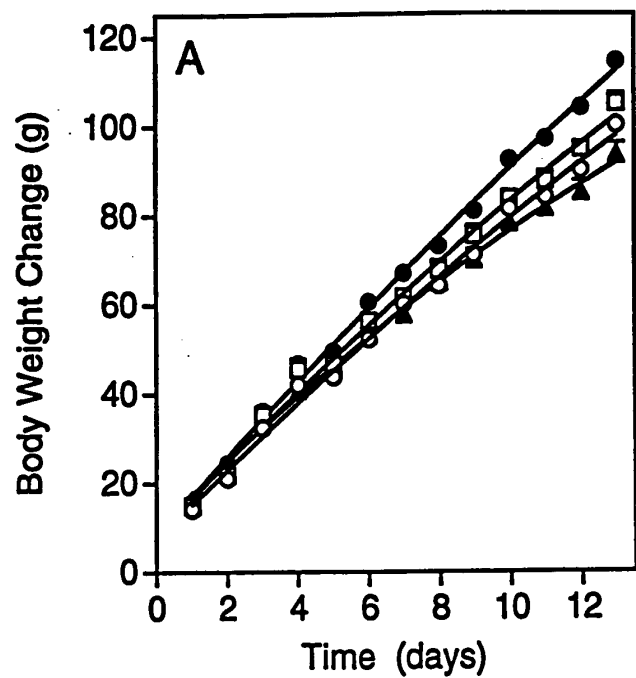






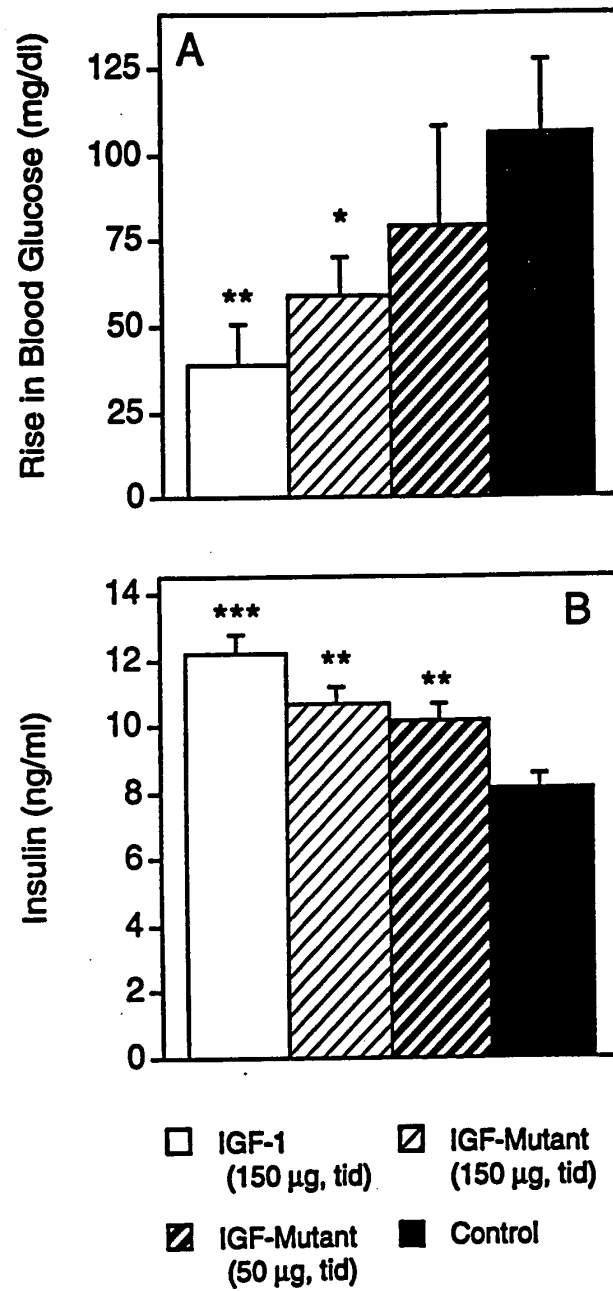
FIG. 21



[illegible]

 IGF-1 (150 µg, tid)
  IGF Mutant (150 µg, tid)

 IGF Mutant (50 µg, tid)
  Excipient Control

[illegible]

plasmid 14.98
length: 5140 (circular)

F16.24

1 GAATTCACACT TCTCCAACTC TTGGATTAAGG AATATACAGC ATGAAATATC TCATTGCTGA GTGTATAT ATCTTCCXC AAAAAGAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCATATCC TTATATGCTG TACTTTTAG AGTAAGACT CAAATATAA TTGAAAGGG TTTTCTCTT TCTGACCTTA
101 GAATGCTGCG CCGAGGTAGA AGCTTTGAG ATTATGCTCA TCGCAATGCT TCGCAATATG GCGCAAAATG ACCAAGAGCG GTTATGAT CAGGTAGAGG
CTTGACACAG GCGTCACATC TCGAAGCTTC TAATAGCAGT GAGGTATGCA AGCTTATAG CCGCTTTTAC TGGTTGTGCG CAATTAAGTA GTCAATCTCC
201 GGGCGCTGTA CGAGTTAAG CCGGATGCCA GCATTCCTGA GAGCATACG GAGCTGCTGC GCGATTAGCT AAAGAGTTA TTGAAGCAT CTGTACATA
CGCGGACAT GCTCATTTTC GGGCTAGGCT CGTAAGACT GGTGCTATGC CTCGAGCAGG CGCTATATGCA TTCTTCAAT AACTGTGAG GAGCAGTAT
301 AAAAGTTAAT CTTTTCACA GCTGTACATA AGTTGTACG GCCCAGACTT ATACTGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCATTA GAAAGTTCT CGACAGTAT TTCAAGCTGC CGGCTCTGAA TATCAGCGAA ACAAAATTA AAATTAACAT AAACATGAT CATGCTTCA
101 TCACGTAAAA AGGATATCTA GAGCTTGAGG TCATTTTATG AAAAAGATA TCCCATTTCT TCTTGCATCT ATGTGCTT TTCTATTC TACAATGCC
AGTCACTTT TCCCATAGAT CTCCAACTCC ACTAAATAG TTTCCTTAT AGCGTAAGA AGAAGTAGA TACAAGCAA AAAGATTAG ATGTTACGG
501 TATGCATCTG GTACCGCCAT GCGTATCCG AACGTTCC GCGGTAAAGA TCTGGCAGGT TCAGCAGCTG GAGCATCCG AGAGGCGCC GAGGTGAGC
ATACGTAGAC CATGGCGTA CCGACTAGG TTGGCAAGG CCGCATTTCT AGACCTCCA AGTGTCCAG CTCCTAGGC TCTCGCGG CTCGACTGC
1 Serp Lythralame Lalaaspro Asnarphes rgllylsas pleuhalagly SerProglys lylylsersi yelylyala glublyaspsp
601 ATCCCGCAA AGCGGCTTT AACTCCCTGC AACCTGAGC GAGCGAATAT ATCGTTATG CGTGGCGAT GGTTGTTGTC ATTGTGCGG CAATATCCG
TAGCGGTTT TCGCGGAAA TTGAGCAGC TTCCGAGTGC CTGCTTATA TACCAATAG GCACCGCTA CCAACACAG TAAAGCCCG GTGATACGC
33 ProAlaly Salalalapha Asnsrleug lhalaserai arhclutyr ileglylra latpalame lvalvalai lilevalgly latrilegly
701 TATCAGCTG TTAAAGAAAT TCACCTCGAA AGCAAGCTGA TAAACGATA CAATTAAGG CTCCTTTG AGCCTTTT TTGGAGAT TTCAAGCTGA
ATAGTCAAC AATCTCTTA AGTGAAGCT TCGTTGACT ATTTGCTAT GTTAATTC CAGGAAGC TCGGAAGAA AACCTCTA AAGTGCAT
66 Ilelyslu Phelyslasp helhsrly salaser
801 AAAATATAT ATTGCAAT CTTTAGTTC TTCTTCTTA TTCTACTCC GCTGAAGTC TTGAAGTTG TTAGCAAA CCGCATACG AAATTCAT
TTTTAATTA TAAGCTTA GAATTCAC AAGAAGAT AACGTGAG GACTTTGAC AACTTCAC AATCGTTT GGGGTATGCT TTTAAGTAA
TACTAAGTC TGAAGAGC ACAAACTTT AGATGTTAC GCTAATATG AGCTTCTCT GTGAATCT ACAGGCTG TAGTTGAC TGTGAGAA
ATGATTCAG AACTTCTGC TGTTCGAAA TCTAGCAATG CGATTGATG TCCCAACAGA CACTTACGA TGTCCGAC ATCAACATG ACCACTGCT
1001 ACTCAGTCTG TAGTAGAGT GCGGTGGCT CTGGTCCGG TGAATTTGAT TATGAAGA TGGCAAGCC TAATAGGGG GCTAGACCG AAATGCCGA
TCAGTCACAG ATCAATCTCA CCGCCACCGA CACCAAGGC ACTAAACTA ATACTTCTT ACGTTTCCG ATTAATCCC CGAATCTGGC TTTACGGCT
1101 TGAAGAGCG CTACAGCTG ACGCTAAGG CAACTTAT TCTGTGCTA CTGATTACG TGTCTATC GATGTTCA TTGTAGCT TTCCGGCTT
ACTTTGCGC GATGTACAG TCGCATTC GTTTAACTA AGACAGCAT GACTATGCC AGAGAGTAG CTACCAAGT AACCTGCA AAGCGCGAA
1201 GCTAATGTA ATGTGCTAC TGTGATTTT GCTGTCTTA ATTCGCAAT GCGTCAGTC GGTAGCGTG ATTAATCAC TTAAATAT AATTCCCTC
CGATTAACAT TACAGCATG ACACATAAA CGACGACAT TAAGCTTTA CCGAGTTAG CCACTGCAC TATTAAGTC AATATCTTA TTAAGCGAG
1301 AATATTTAC TTCCCTCCCT CAATCGTTG AATGTGCC TTTTGTCTT AGCGTGTGA AACCATAGA ATTTCTAT GATTGACA AATTAACCT
TTATTAATG AAGGAGGGA GTTAGCAAC TTACAGCGG AAACAGAAA TCGGACCAT TTGTATCT TAAAGATA CTAACCTCT TTATTTGAA
1401 ATTCGCTGT GTCTTCCCT TTCTTTATA TGTTCGACC TTATGTATG TATTTCTAC GTTGTGAC ATACTGCTA ATAGAGTC TTAATCAGC
TAAAGCAACA CAGAAAGCA AAGAAATAT ACAAGCTGAG AATTAATATC ATTAAGATG CAAAGATTC TATAGCGAT TATCTCAG AATTAATAGC

3201 ACTCAAGGC GTTATATACGG TTATCCACAG AATCAGGGGA TAAAGCAGGA AAGAACATGT GAGCMAAAG CCAGCMAAG GCCAGAACCC GTMAAAGGC
TGAGTTTCG CCAATATAGCC AATAGGTGTC TTACTCCCTT ATTGCTCCCT TCTCTGTACA CAGCTTTTCG GGTGCTTTTC CCGTCTTCG CATTITTCG
3301 CGUUTTCCTG GCGTTTTTCC ATAGCTCCG CCCCCCTGAC GAGCATGACA AAATCGAGC CTCAGTACG AGGTGGCGAA ACCCGACAGG ACTATMAAGA
GGCGAAGCAG CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTACTGT TTTTAGCTGC GAGTTCACTC TCCACCGCTT TGGGTGTCG TGNATTTCT
3401 TACAGAGCGT TTCCCCCTGG MAGTCCCTC GTGCGCTTC CTGTCCGAG CCIAGCGCTT ACCGATACG TGTCCGCTT TCTCCCTTCG GAGCGCTGC
ATGCTCCGCA AAGCGGAGCC TTCCAGGAGG CAGCGAGAG CAGAGGCTG GAGCGGCGAA TGGCTATAGG ACAGCGCGAA AAGAGGAGC CTTCCGACC
3501 GCGTTTCTCA TAGCTCAGCG TGTAGTATC TCACTCCGT GTAGTCTGT CCGTCCAGC TGGGCTGTGT GCACGMAACC CCGTTACG CCGACCGCTG
GCCAAGAGT ATCGATGCG ACATCCATAG AGTCMAAGCA CATCCAGCA GCGAGGTTG ACCCGACACA CTTGCTTGGG GCGCAGTGG GCTTGGGAGC
3601 GCGCTTATCC GGTACTATC GTCTTACATC CAACCCGCTA AGACAGGACT TATCGCACT GCGCAGAGC ACTGCTACA GATTAACAG AGCGAGTAT
GGGGAATAGG CCAATGATAG CAGAACTAG GTTGGGCTAT TCTGTCTCA ATAGCGGTGA CCGTCTCGG TGACCAATGT CCAATGCTC TCGCTCATAT
3701 GTAGCGGCTG CTACAGATT CTTCAGTGC TCGCTTACT AGGCTACAC TAGAAGACA GTATTGCTA TCTGCGCTCT GTGMAAGCA GTTACTCTG
CATCGGCCAC GATCTTCA GAACTTACG ACGGATTTGA TCGGATGAG ATCTTCTGT CATMAACAT AGACCGGAGA CGACTTGGT CAATGGAAGC
3801 GAAAAAGAT TGTAGCTCT TGAATCCGCA AACMAACAC CGCTGTAGC GGTGTTTTT TTGTTTGA GAGCAGATT ACCGCGAGAA AAAAAGATC
CTTTTCTCA ACCATGAGA ACTAGCGCT TGTTTGAG GCGACCATG CCACCAAAA MCMAAGCTI CGTGTCTMA TCGCGCTCT TTTTCTTAG
3901 TCMAAGAT CCTTGATCT TTCTACGGG GTCTAGCCT CAGTGGAGC AAAACTAGC TTAAGGATT TTGCTCATGA CATTATCAA AAGATCTTC
AGTCTCTCA GMAAGTACA AAGATGCCC CAGACTCGA GTACCTTGC TTGTAGTGC AATTCCTMA AACCACTACT CTAAATGTT TTCTTAGAG
4001 AACTAGTCC TTTTAATTA AAATGAGT TTTAATCAA TCTAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTACCA ATCTTAATC AGTAGAGCAG
TGATCTAGG AAATTTAAT TTTTACTTCA AAATTAGT AGATTCTATA TAACTCAT TGAACAGAG TGTCAATGT TAGAATTAG TCACTCCGTG
4101 CTATCTACG GATCTCTCA TTCTGTCA CCATAGTTCG CAGACTCCG CTCTGTGTA TAACTAGAT AACGAGAGG TTAACATCTG GCCCAGTGC
GATAGAGTGC CTAGACAGAT AAGCMAAGTA GGTATGACG CACTAGGGG CAGACATCT ATTGATGCTA TCCCTCCCG AATCTAGAG CCGGGTACG
4201 TGCATATTA CCGGAGAGC CAGGCTACG GCTCCAGAT TTATCAGCA TAAACAGCC AGCCGAGAG GCCCAGCGCA GAGTGTGC TGCACCTTA
AGTTACTAT GCGGCTTGG GTGAGTGG CCGAGGTCA AATAGTCTT ATTGGTGG TCGGCTTCC CCGCTCGCT CTTCACAGG ACCTGAAT
TCCGCTTCCA TCCAGTCTAT TAACTCTGC CCGCAGCTA GAGTAGTNG TTCGCACTT AATAGTTTC GCAACCTGT TGCATCTCT GCAAGCATG
AGCGGAGCT AGCTAGATA ATTACAGAG GCGCTTCAAT CTCAATTATC AAGCGTCA TTTTCAAGC CATTGACAA AGCTGAGC
4301 TGGTGTACG CTCGTGCTT GGTATGCTT CATTCAGTGC CCGTCCCA CGATCAGGC GAGTACATG ATCCCCATG TTGTCAAAA AAGCGTTAG
ACCAAGTGC GAGCAGCAA CCATACCGAA GTAGTGCAG GCCAAGGCT GCTAGTCCG CTCAATGAC TAGGGGTAG AACAAGTTT TTGSCCATC
4501 CTCCTCGCT CCTCCGATG TGTGAGAG TAACTGGCC GCACTGTAT CACTATGCT TATGGCAGA CTGCATAT CTCTACTGT CATGCCATC
GAGGAGCCA GAGGCTAGC AACAATCTC ATTCAAGCG CGTCAATA GTAGATACA ATACGCTGT GACGTATTA GAGATGACA GTAGGTAGG
4601 GTAAGATCT TTTCTGTAC TGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTATG CCGCAGCCA GTTGTCTG CCGCGCTCA ACAGGGATA
CATCTVAGA AAGACACTG ACCACTAGT AGTGTGTCA GTAGACTCT TATCACAATAC GCGCTGCT CAACAGAG GGGCGGAGT TGTGCCAT
4701 ATACCGGCG ACATAGACA ACTTAAAG TGTCACTAT TGGMAAGT TCTTGGGGG GMAATCTC AAGATCTTA CCGGTGTGA GATCAGTTC
TATGGCGCG TGTATGCT TCAAAATTC ACCAGTAGA ACTTPTCA AGAGCCCG CTTTACAG TTCTAGAT GCGCAACT CTAGCTAG
4801 GATGTAAAC ACTGTGAC CCACTGATC TTGACATCT TTTACTTCA CAGCGTTTC TGGGTAGCA AAAAAAGAA GCGMAATGC CCGMAAAG
CTACATTGG TGAACAGTG GGTGACTAG MATTCCTAGA AATGAAGT GGTGCTAG AGCACTGT TTTGTCTT CAGTTTACG GCGTTTTTC

FIG. 25

**gene-8 Naive Library Enrichments:
Selection using 4 Library Pools Each**

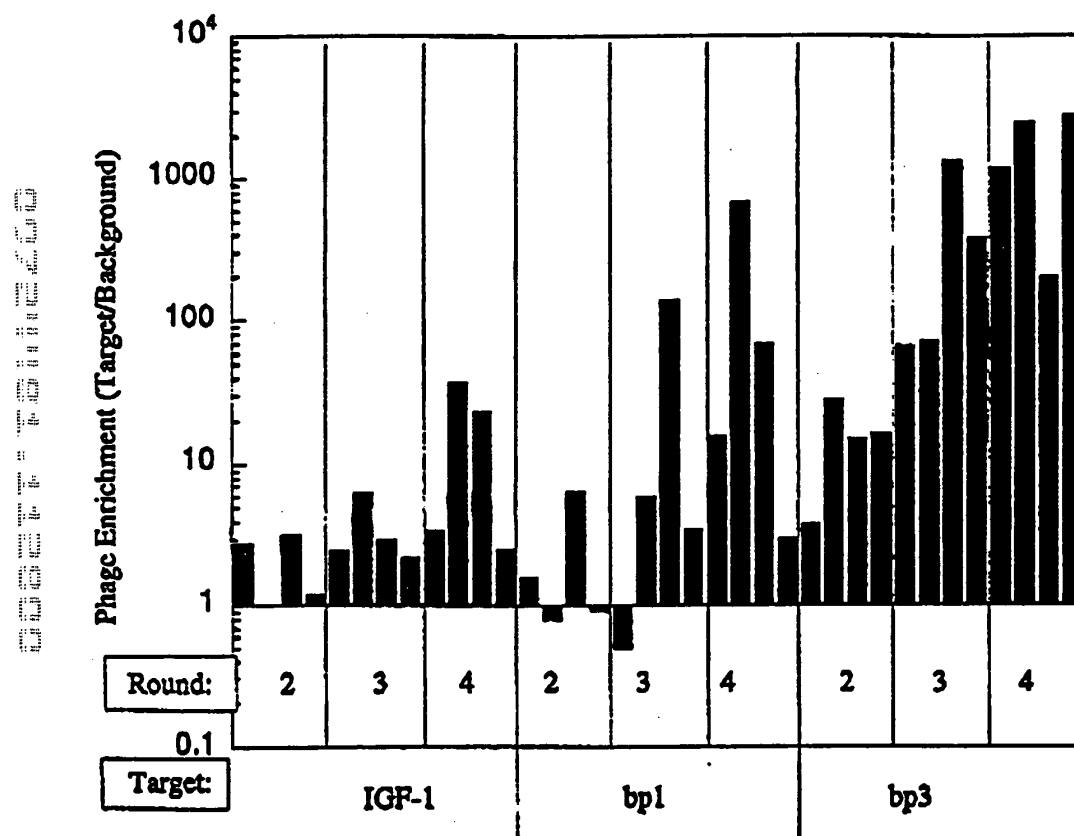


FIG. 26

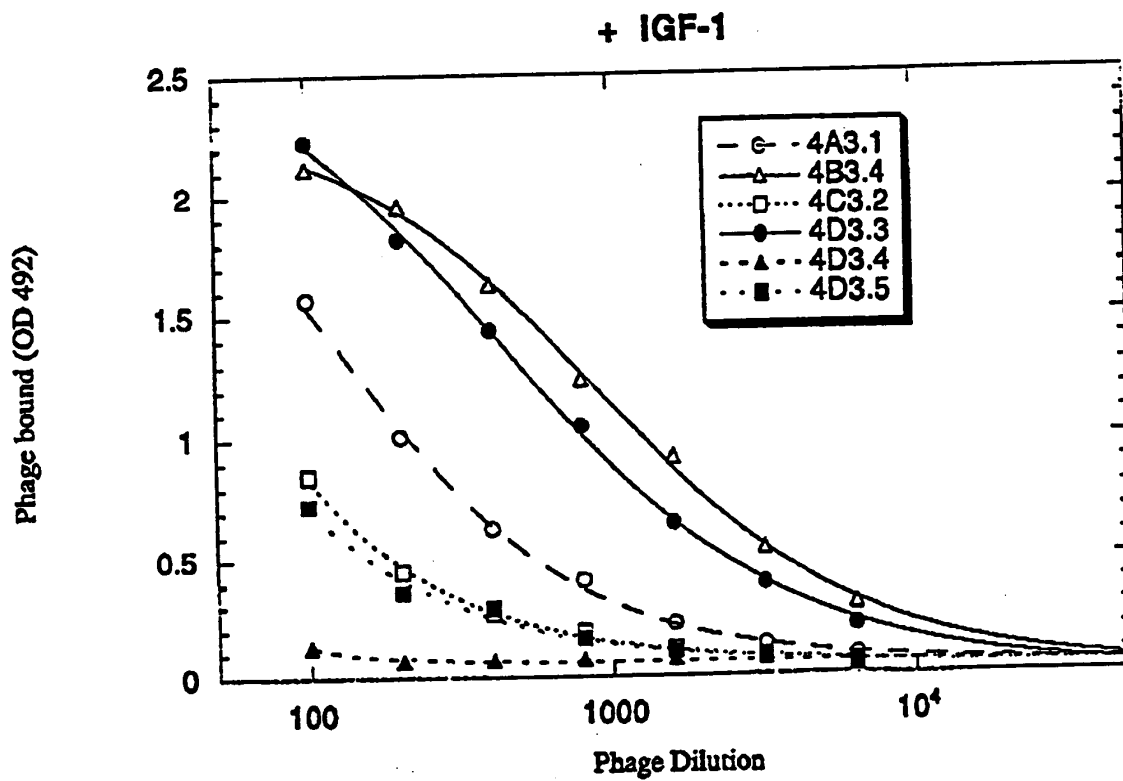


FIG. 27

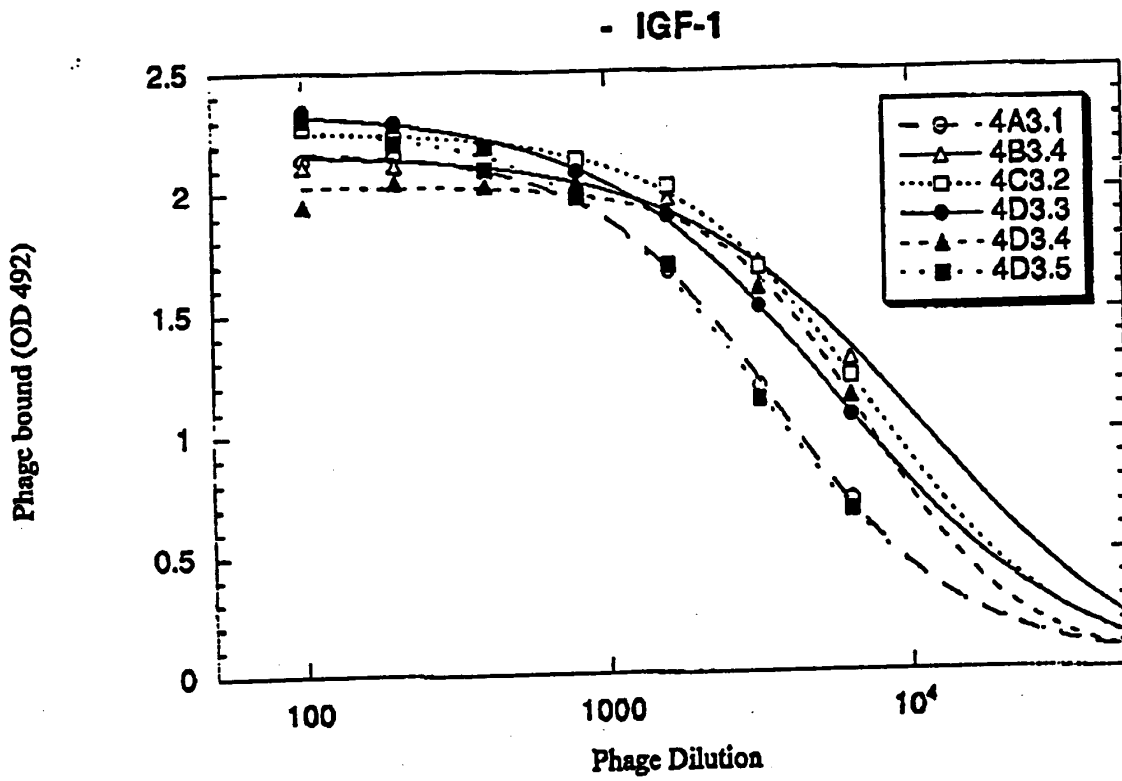
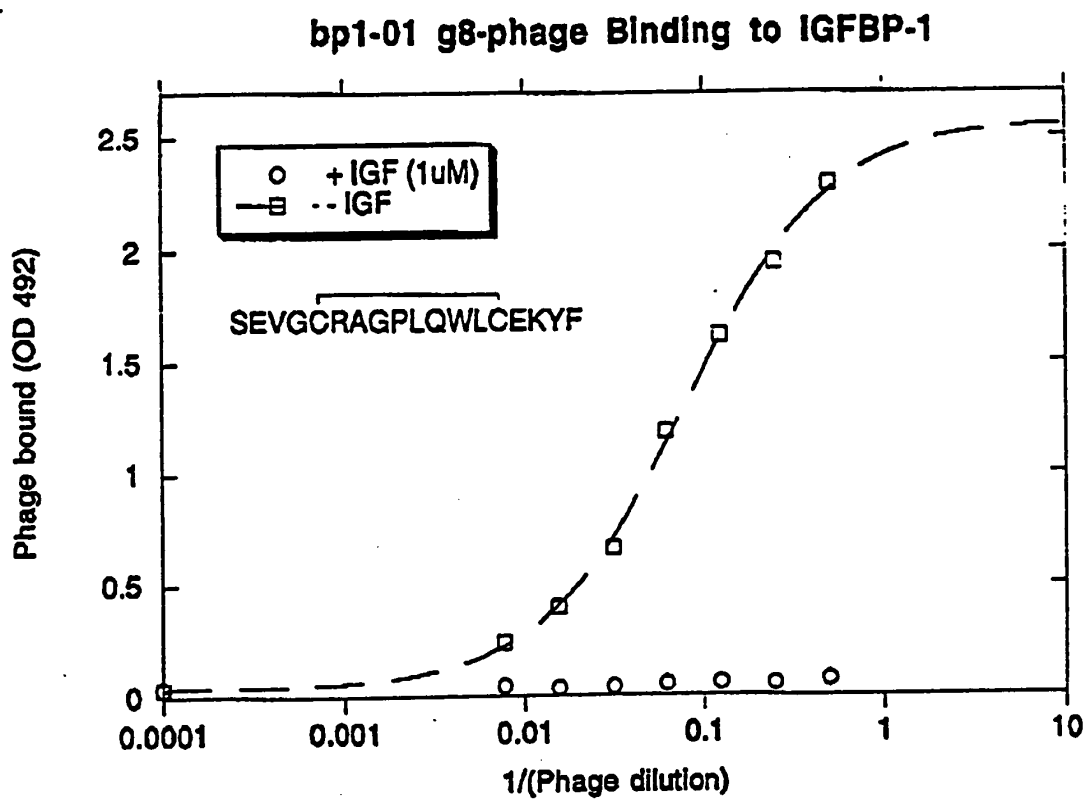


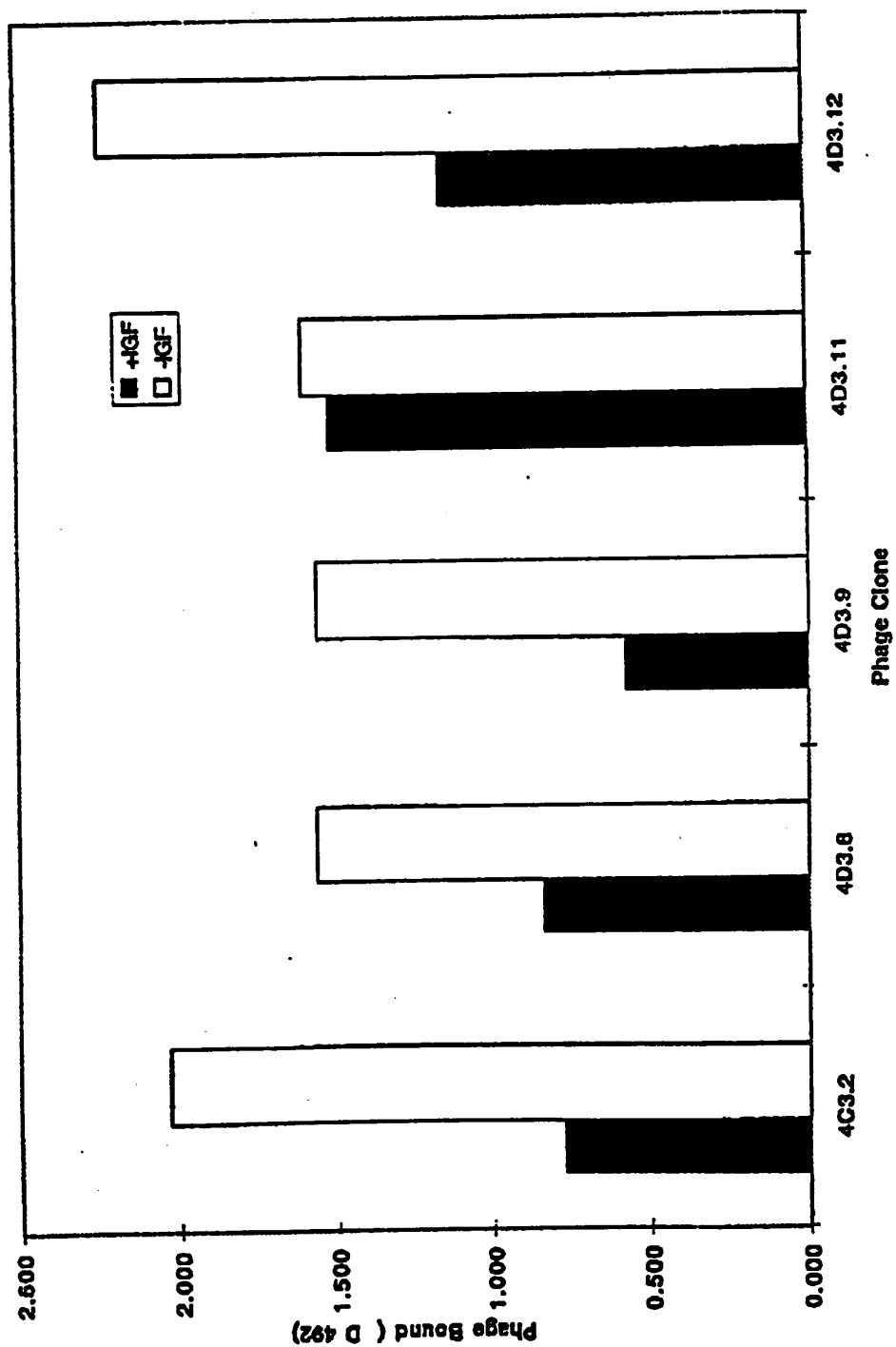
FIG. 28



000007 7011200

FIG. 29

(A) PHAGE BLOCKING ASSAY



SECRET - FROTHING

FIG. 30

(B) PHAGE IGF BLOCKING ASSAY

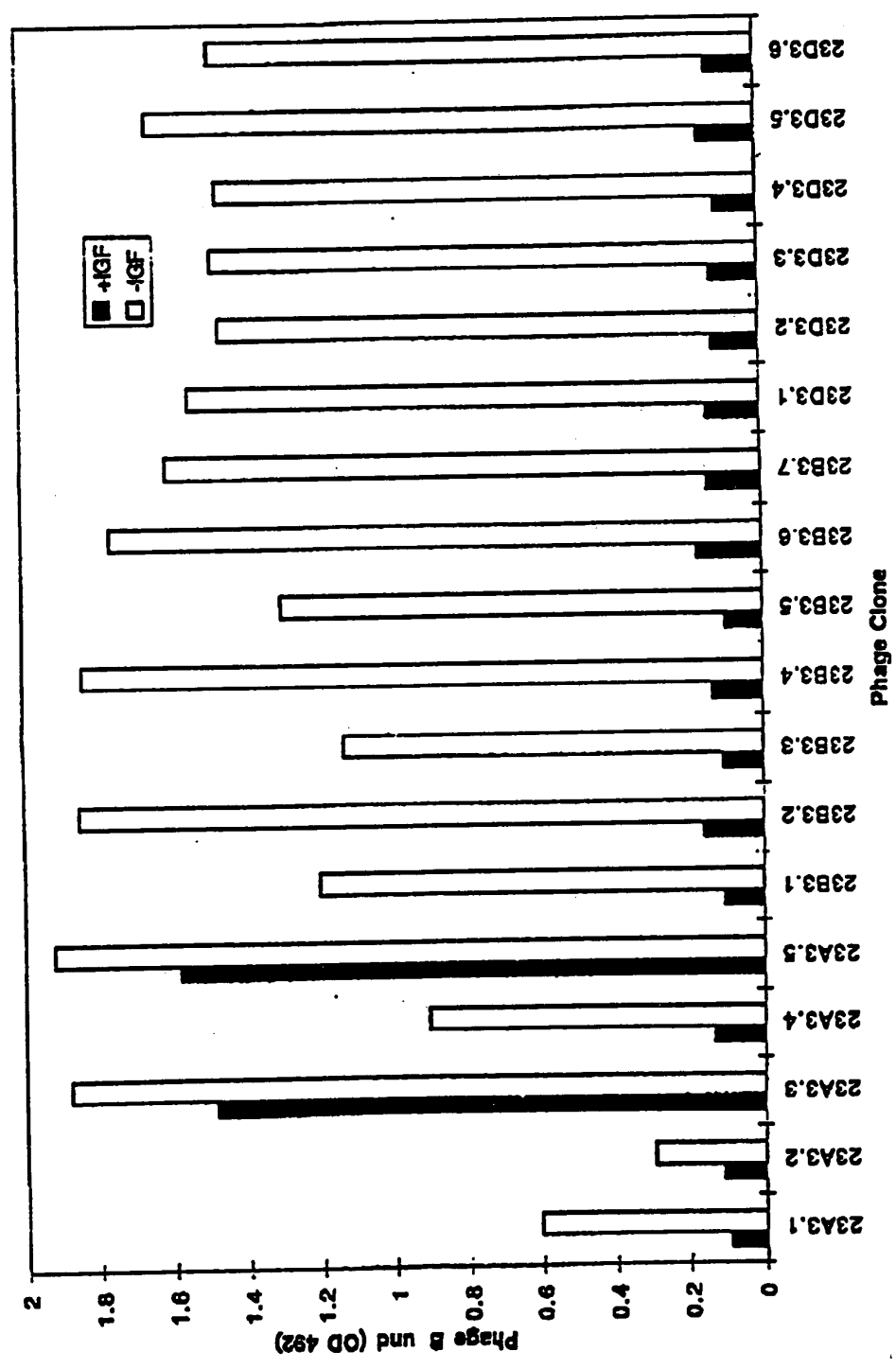


FIG. 31

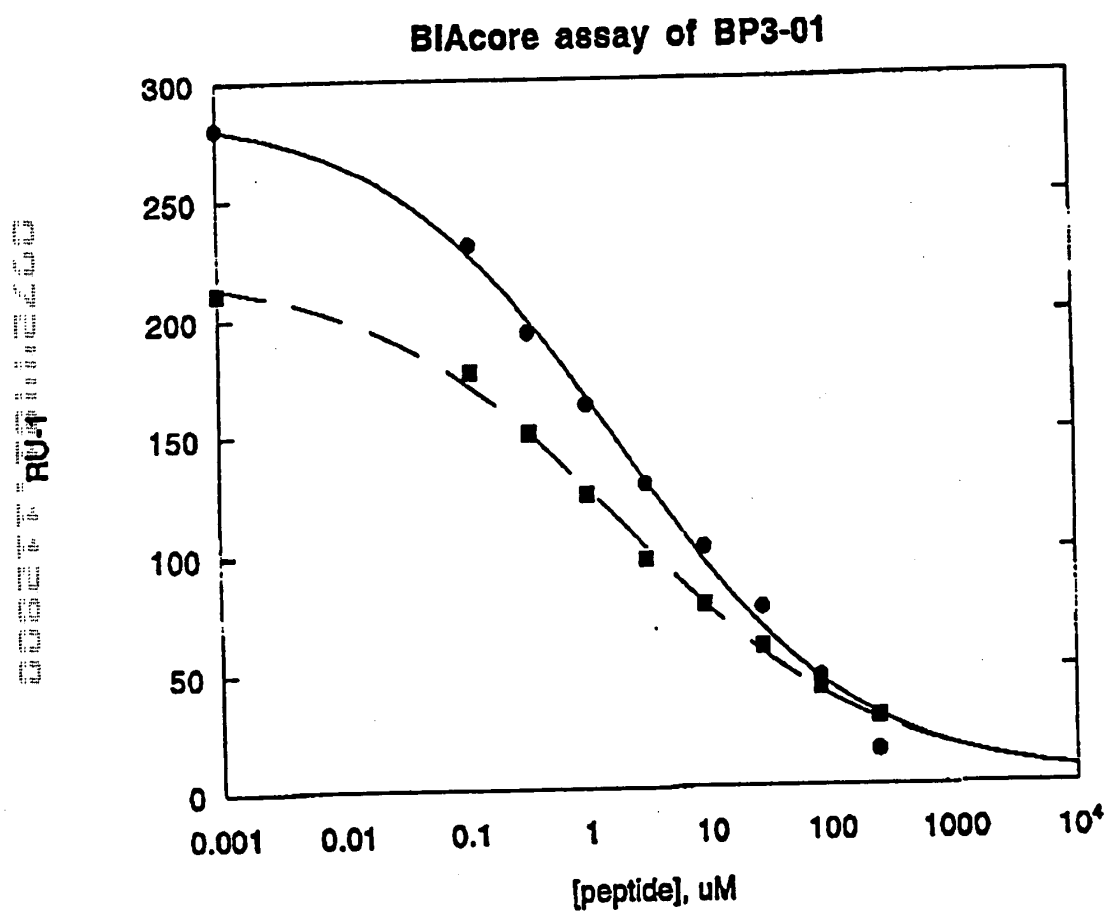


FIG. 32

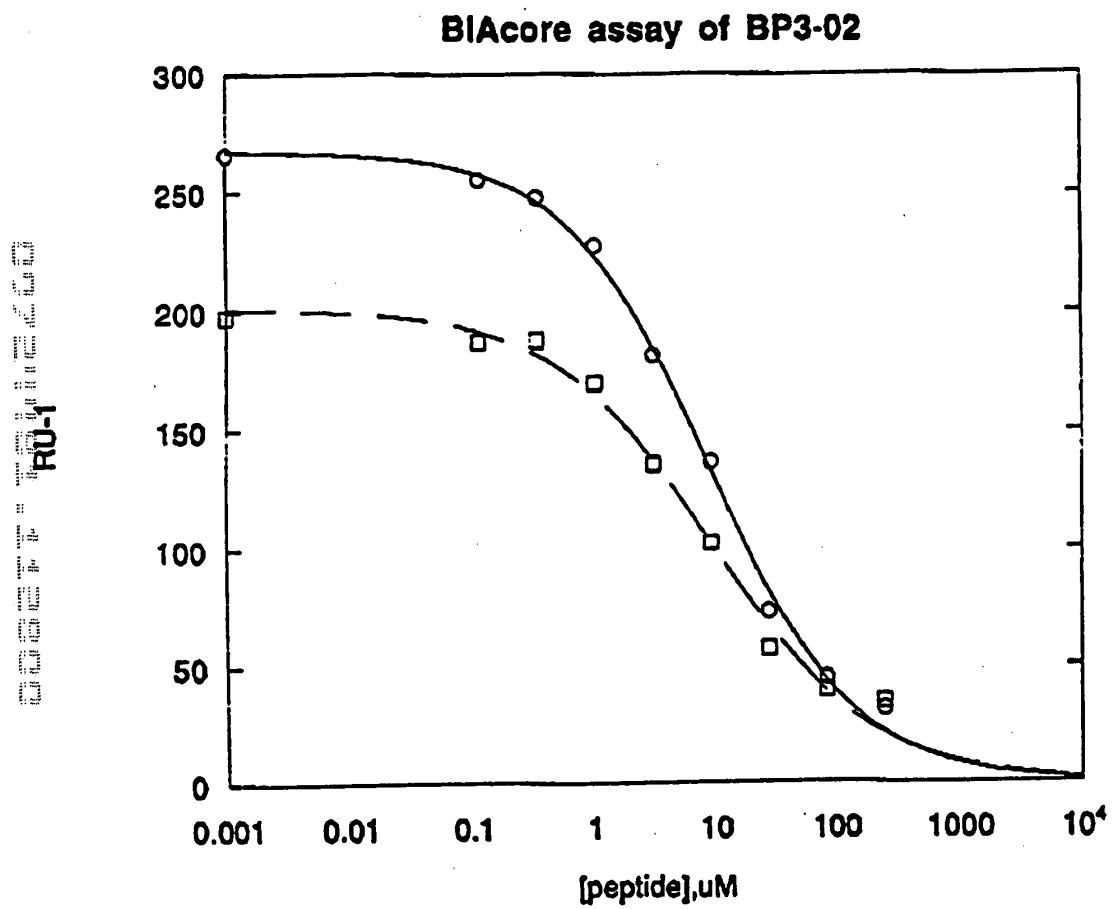


FIG. 33

Inhibition of biotin-IGFBP-1 Binding to IGF-1

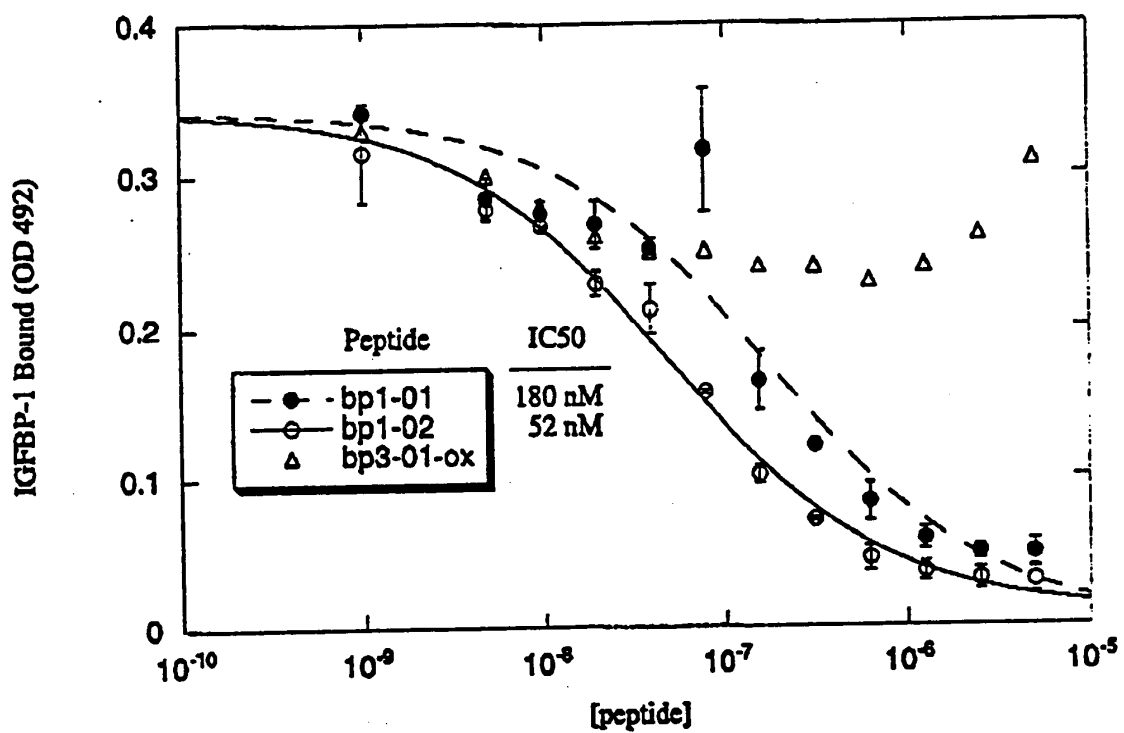


FIG. 34

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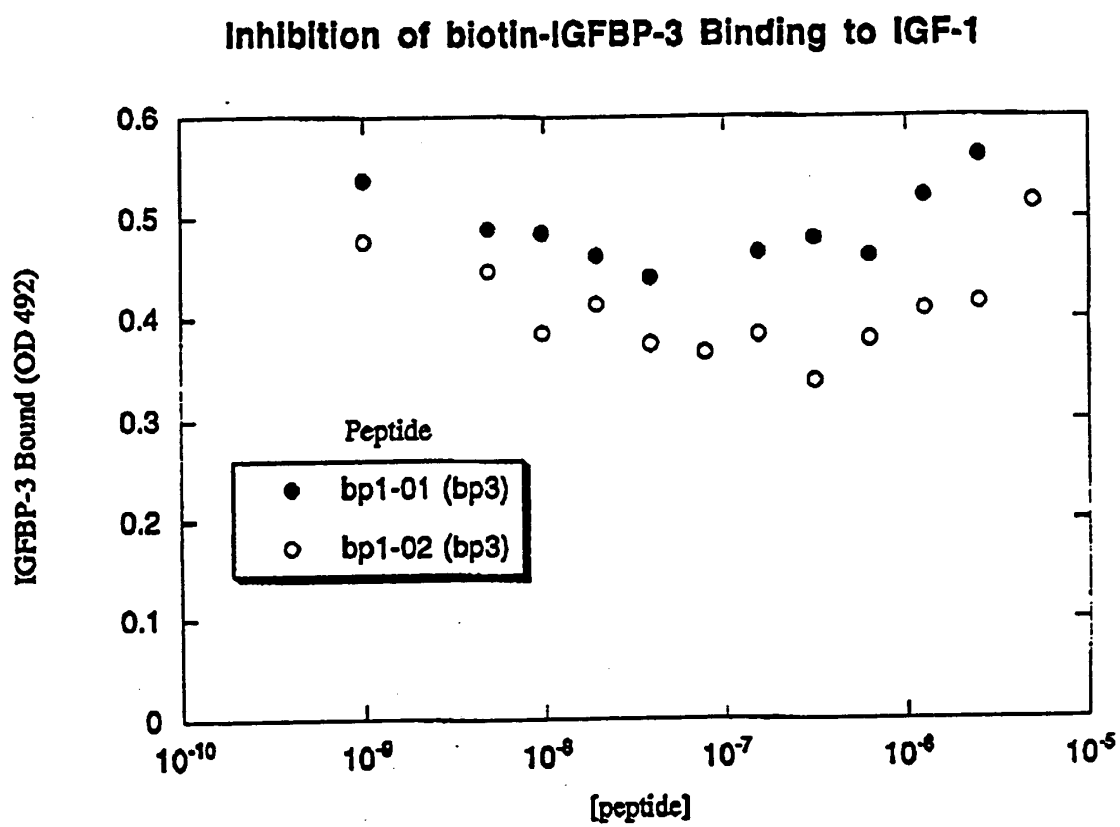


FIG. 35

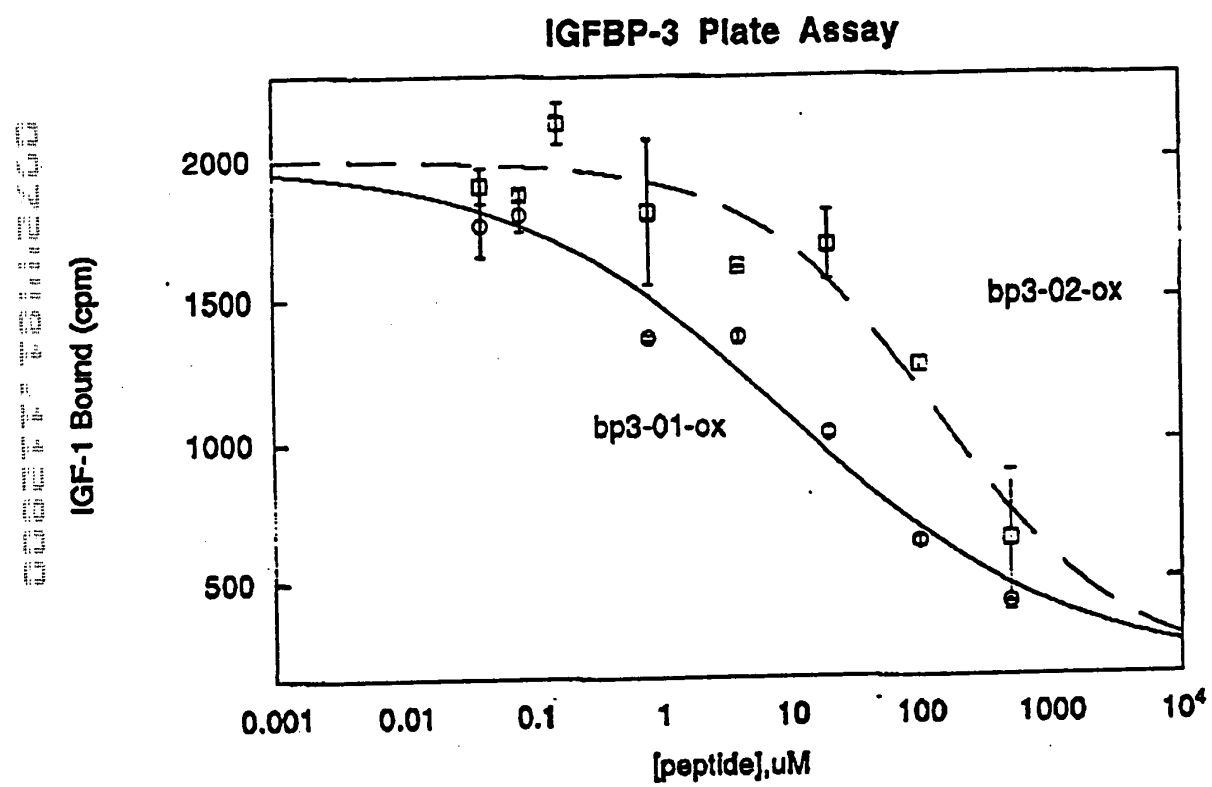


FIG. 36

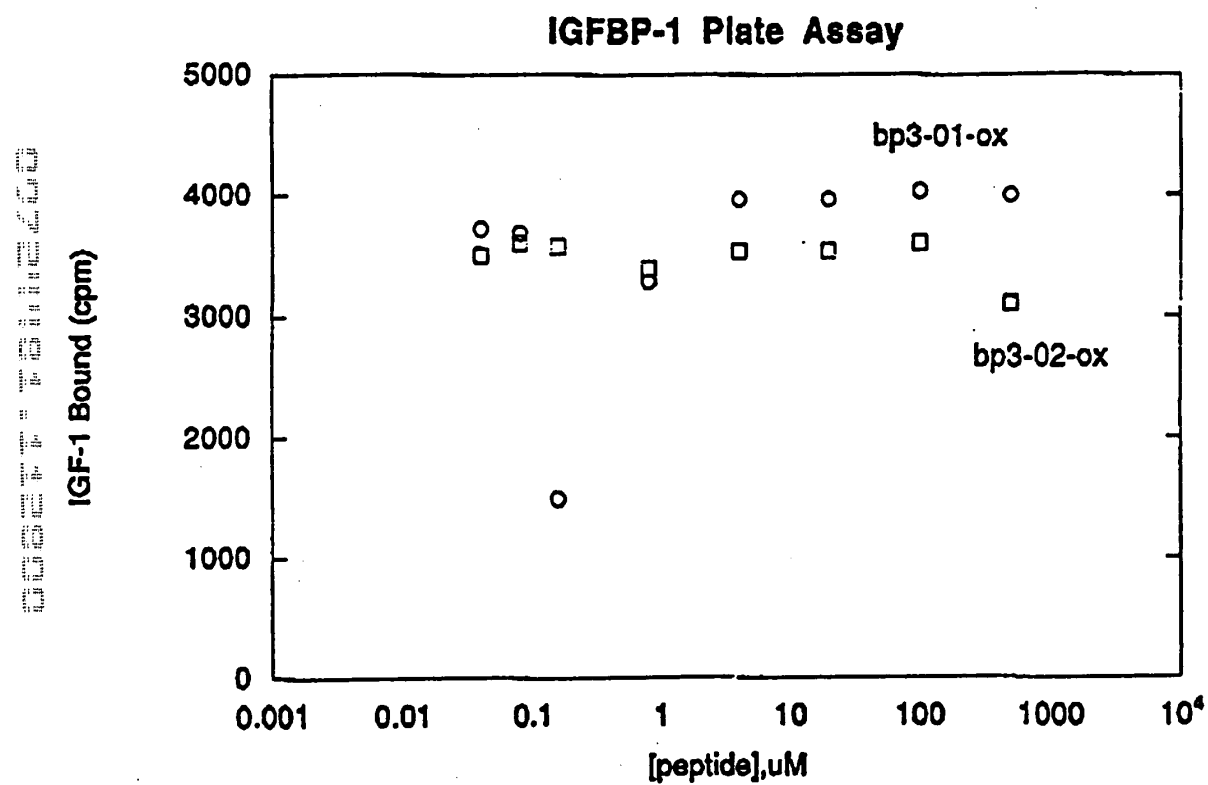


FIG. 37

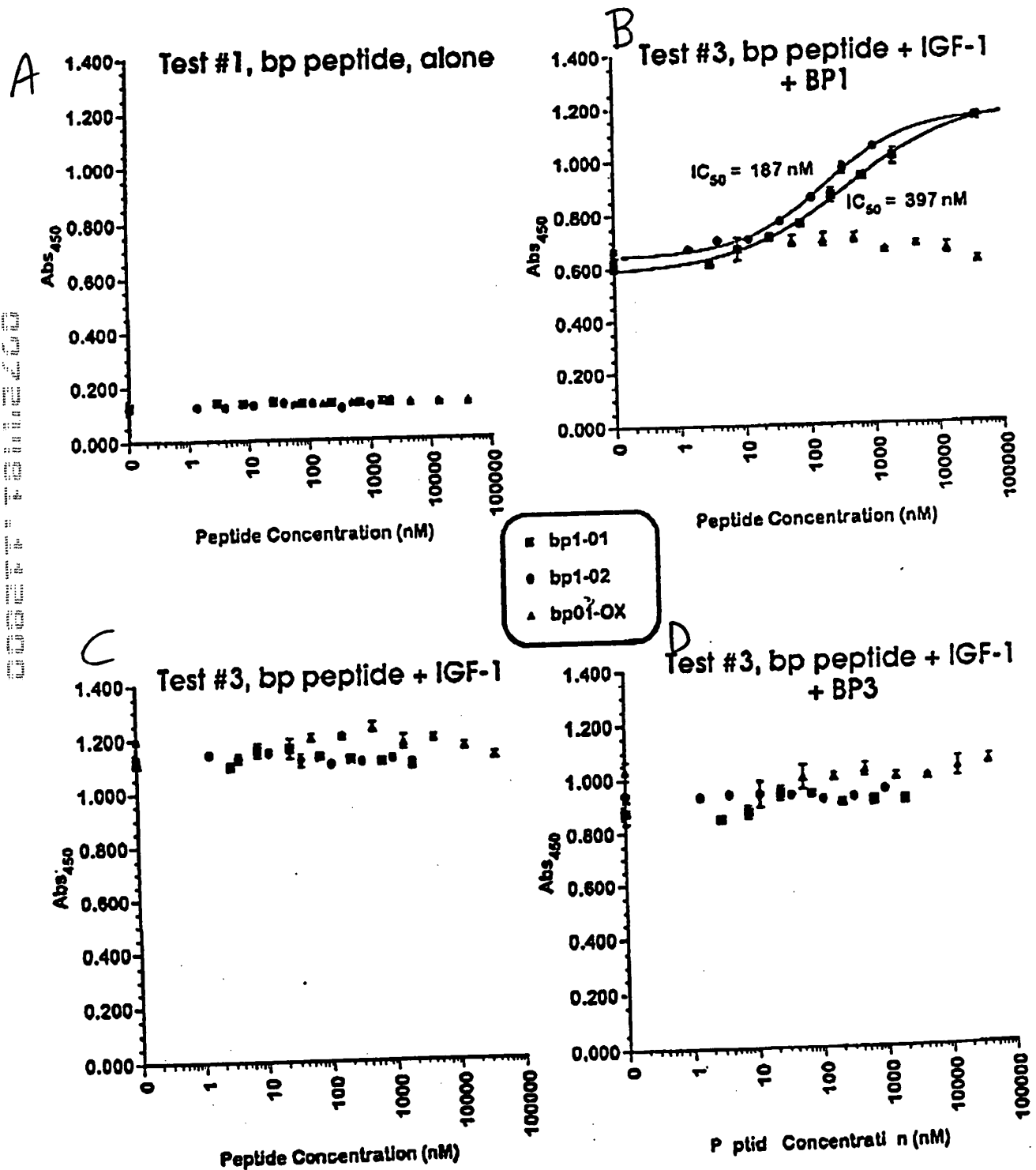
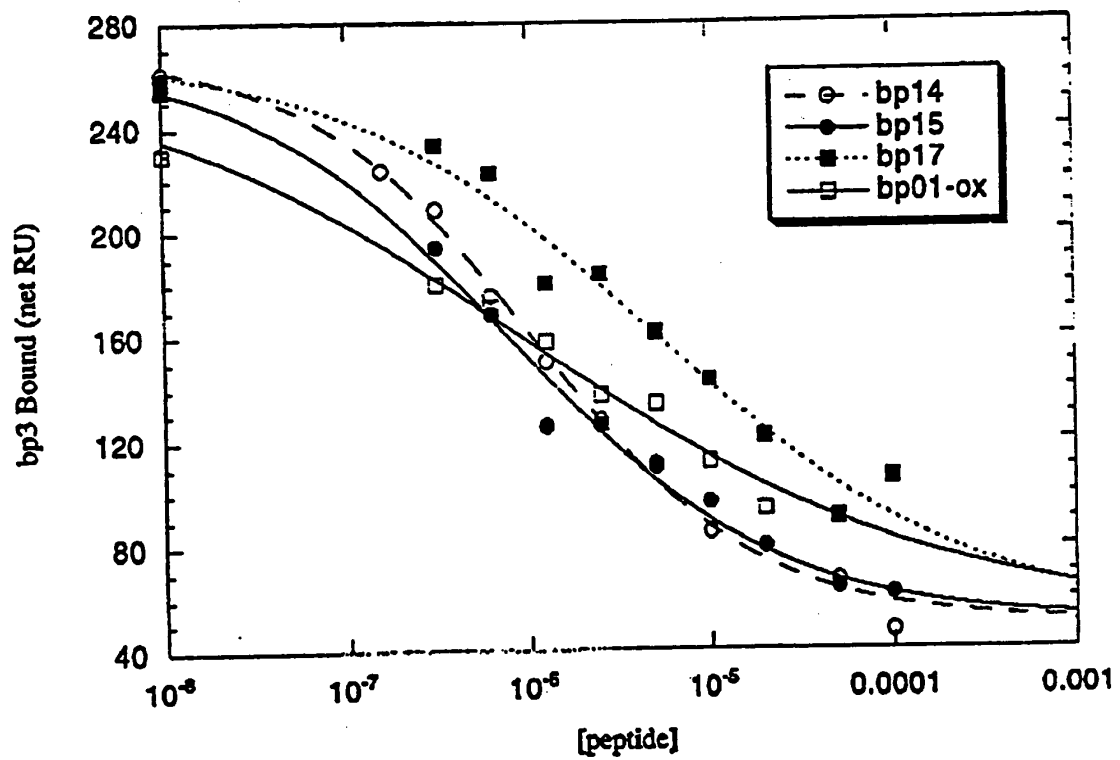


FIG. 38

Competition with 20 nM IGFBP-3
for Binding to Immobilized IGF-2



DATE	DESCRIPTION	AMOUNT	BALANCE
1900	Jan 1		100.00
	Feb 1	50.00	150.00
	Mar 1	25.00	175.00
	Apr 1	75.00	250.00
	May 1	100.00	350.00
	Jun 1	150.00	500.00
	Jul 1	200.00	700.00
	Aug 1	250.00	950.00
	Sep 1	300.00	1250.00
	Oct 1	350.00	1600.00
	Nov 1	400.00	2000.00
	Dec 1	450.00	2450.00
1901	Jan 1	500.00	2950.00
	Feb 1	550.00	3500.00
	Mar 1	600.00	4100.00
	Apr 1	650.00	4750.00
	May 1	700.00	5450.00
	Jun 1	750.00	6200.00
	Jul 1	800.00	7000.00
	Aug 1	850.00	7850.00
	Sep 1	900.00	8750.00
	Oct 1	950.00	9700.00
	Nov 1	1000.00	10700.00
	Dec 1	1050.00	11750.00
1902	Jan 1	1100.00	12850.00
	Feb 1	1150.00	14000.00
	Mar 1	1200.00	15200.00
	Apr 1	1250.00	16450.00
	May 1	1300.00	17750.00
	Jun 1	1350.00	19100.00
	Jul 1	1400.00	20500.00
	Aug 1	1450.00	21950.00
	Sep 1	1500.00	23450.00
	Oct 1	1550.00	25000.00
	Nov 1	1600.00	26600.00
	Dec 1	1650.00	28250.00
1903	Jan 1	1700.00	29950.00
	Feb 1	1750.00	31700.00
	Mar 1	1800.00	33500.00
	Apr 1	1850.00	35350.00
	May 1	1900.00	37250.00
	Jun 1	1950.00	39200.00
	Jul 1	2000.00	41200.00
	Aug 1	2050.00	43250.00
	Sep 1	2100.00	45350.00
	Oct 1	2150.00	47500.00
	Nov 1	2200.00	49700.00
	Dec 1	2250.00	51950.00
1904	Jan 1	2300.00	54250.00
	Feb 1	2350.00	56600.00
	Mar 1	2400.00	59000.00
	Apr 1	2450.00	61450.00
	May 1	2500.00	63950.00
	Jun 1	2550.00	66500.00
	Jul 1	2600.00	69100.00
	Aug 1	2650.00	71750.00
	Sep 1	2700.00	74450.00
	Oct 1	2750.00	77200.00
	Nov 1	2800.00	80000.00
	Dec 1	2850.00	82850.00
1905	Jan 1	2900.00	85750.00
	Feb 1	2950.00	88700.00
	Mar 1	3000.00	91700.00
	Apr 1	3050.00	94750.00
	May 1	3100.00	97850.00
	Jun 1	3150.00	101000.00
	Jul 1	3200.00	104200.00
	Aug 1	3250.00	107450.00
	Sep 1	3300.00	110750.00
	Oct 1	3350.00	114100.00
	Nov 1	3400.00	117500.00
	Dec 1	3450.00	120950.00
1906	Jan 1	3500.00	124450.00
	Feb 1	3550.00	128000.00
	Mar 1	3600.00	131600.00
	Apr 1	3650.00	135250.00
	May 1	3700.00	138950.00
	Jun 1	3750.00	142700.00
	Jul 1	3800.00	146500.00
	Aug 1	3850.00	150350.00
	Sep 1	3900.00	154250.00
	Oct 1	3950.00	158200.00
	Nov 1	4000.00	162200.00
	Dec 1	4050.00	166250.00
1907	Jan 1</		

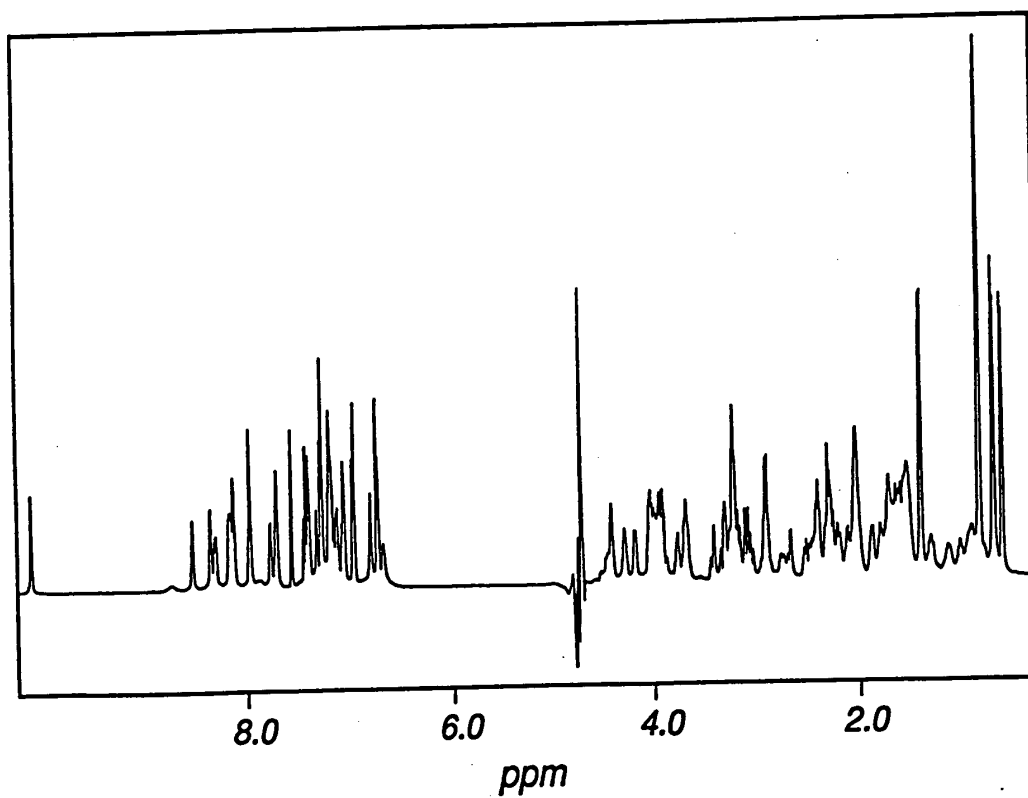
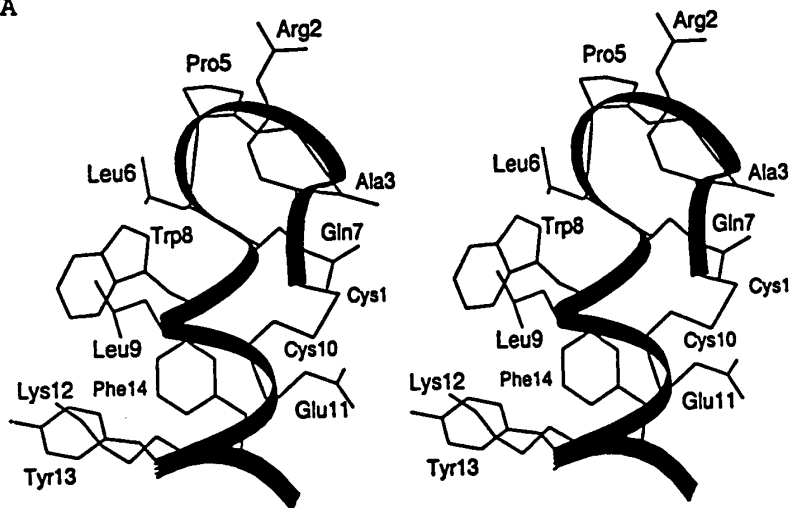


FIG. 40

A



B

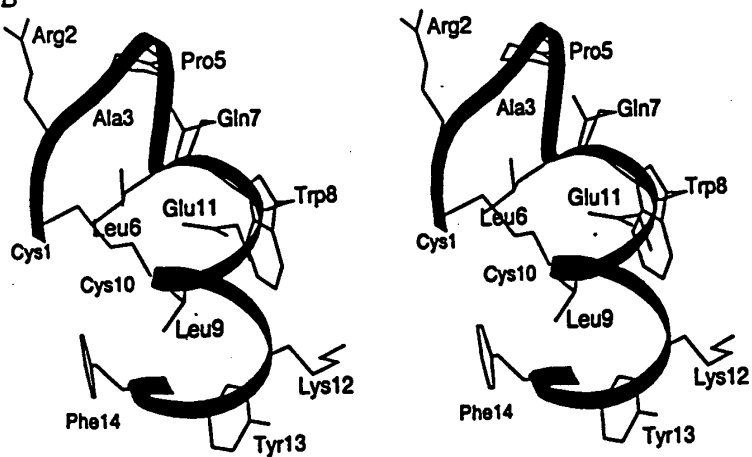


FIG. 41

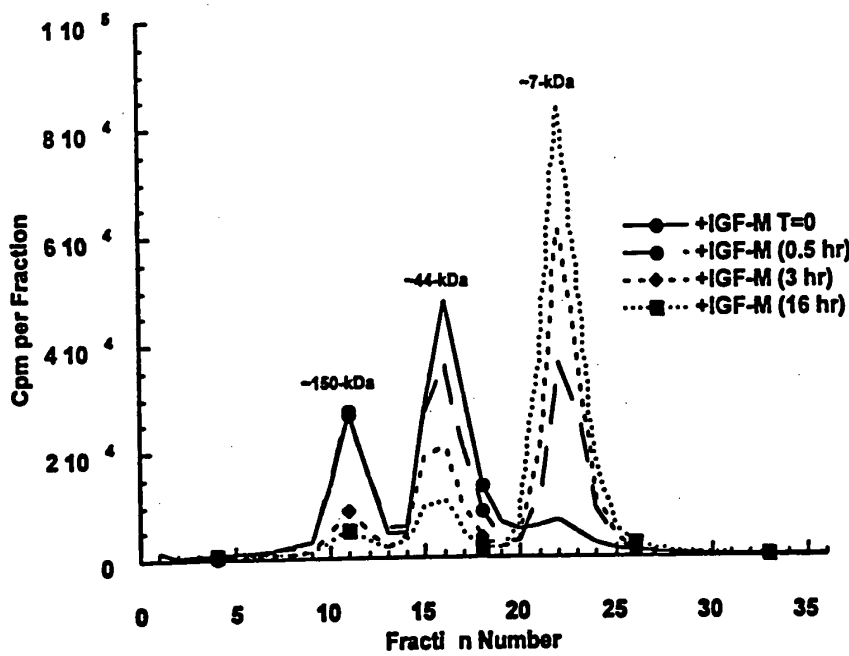
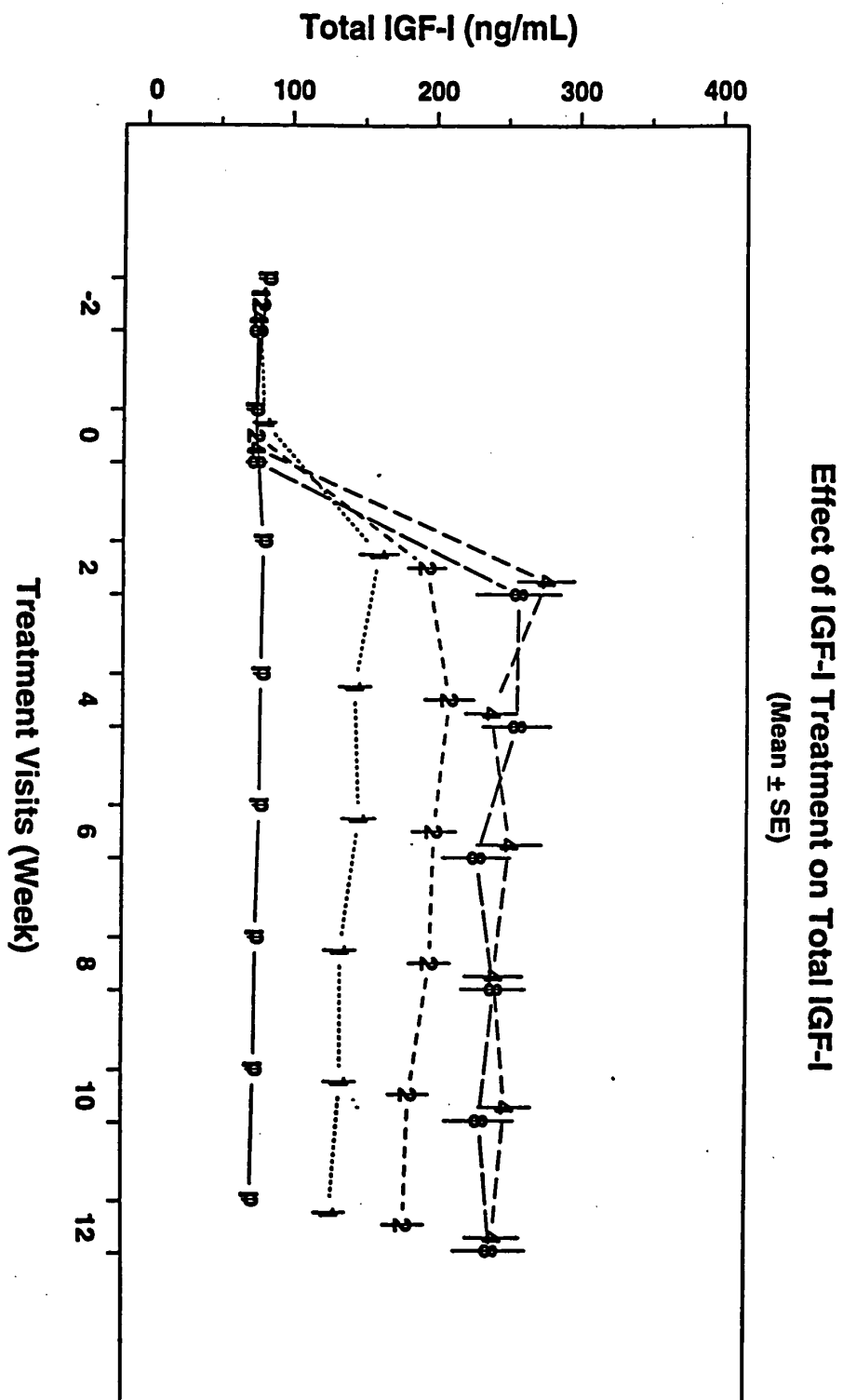
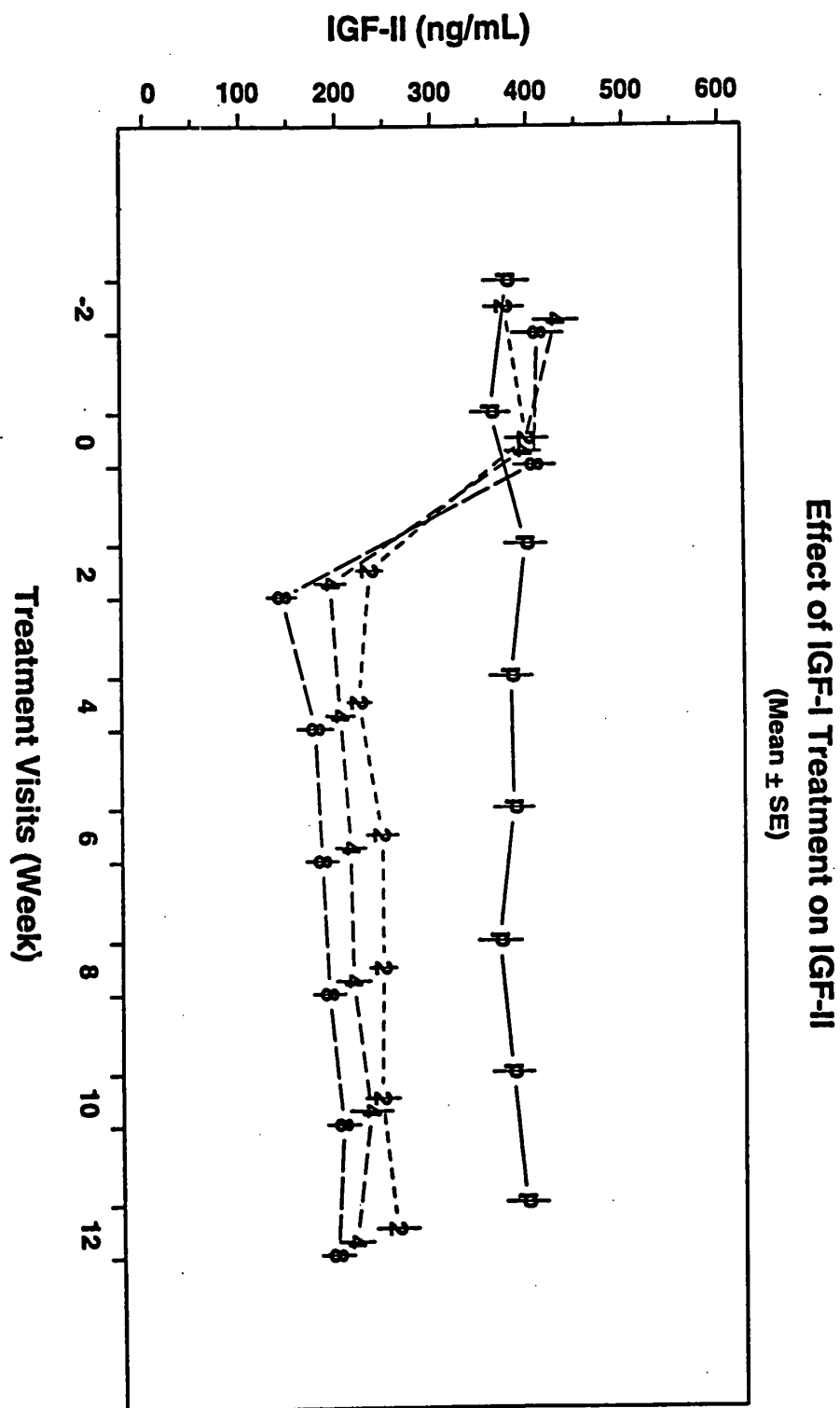


FIG. 42



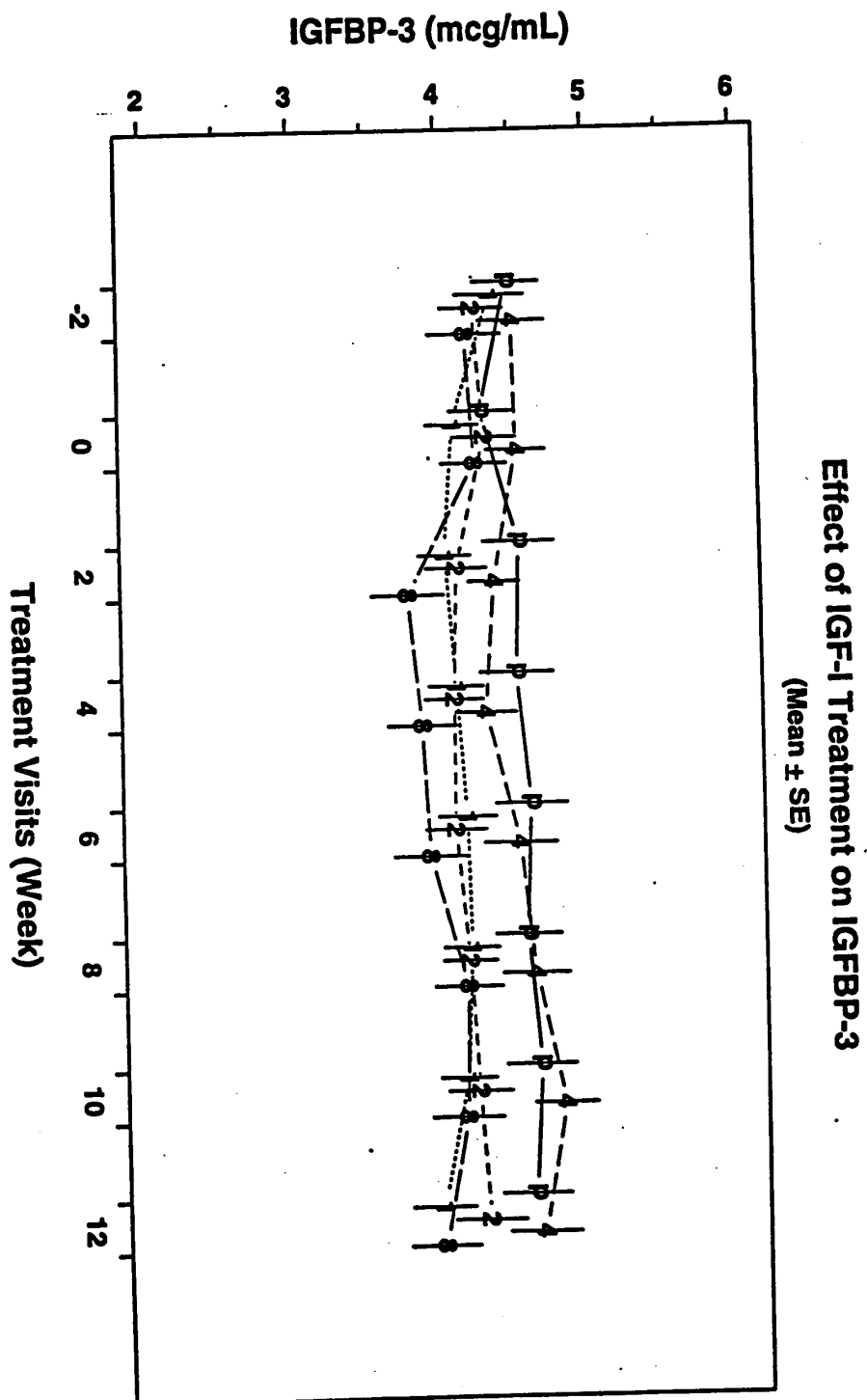
00721104-443000

FIG. 43



00221191.113000

FIG. 44



007341104 443000